ARCHIVES OF SURGERY

VOLUME 49 NOVEMBER 1944 NUMBER 5

COPYRIGHT, 1944, BY THE AMERICAN MEDICAL ASSOCIATION

GENETIC ASPECTS OF THE CANCER PROBLEM

PRELIMINARY REPORT ON A SURVEY OF CONSTITUTION AS RELATED TO CANCER

FRITZ BLANK, M.D.

NEW YORK

FOREWORD

F. A. E. CREW, M.D., F.R.S.

This survey of the biologic background of cancer is the first major attempt by this institute (the Bureau of Human Heredity) to present the results which can be achieved through the clearing house method. It has been made possible by international collaboration between the Bureau of Human Heredity and the Genetics Laboratory of Ohio State University. Both institutes are foci of much friendly cooperation between individual workers and numerous institutes.

It is worth noting that the work was begun in London in 1940—the period of constant day and night air raids—and (owing to that fact) was transferred at short notice to the friendly institute which has fathered its completion. Enemy action caused three hundred references to be lost in transit, which were later replaced from duplicates.

The Bureau of Human Heredity has been evolving the mechanism for such work as this on the most fully international lines since it opened in 1936.

There are three main functions of the clearing house, or information center:

1. References—that is, an extensive bibliography—are collected.
2. Added to these are fully indexed data collected from separates and information sent in by individual research workers, approached by a wide correspondence plan.
3. Information on the preceding data is furnished on request, so that the needs of the individual enquirer are dealt with. (Publication does not form part of the work, since new data, arriving steadily, modify previous findings.) Information rests on comparative analysis of the data collected.

Analysis, moreover, entails the collection of papers on diagnosis and case histories; further, careful definition of terms is required, which results in an impressive body of information on nomenclature—this has now been developed as a Synonyma Index. It throws light both on the data and on the usage of different schools; differences are observed not only between one part of the world and another but often within the same country. The crux of the work thus briefly described is the method of the cross reference index, best compared to a great sorting machine. The desideratum was outlined early by R. A. Fisher and J. B. S. Haldane in consultation. It works well. Three thousand sections on constitution and traits were already available when Dr. Blank began the cancer collection. Points in the present survey can be set against a further fifteen hundred odd.

Many papers on heredity in cancer called for special treatment and could not be dealt with apart from comprehensive study of the biologic background, including variations of constitution, as viewed by research workers. Some correlation with medical observations on case histories has been possible. This preliminary survey aims at assessing the knowledge (as it stood in 1941) on interaction of organic and inorganic forces found in various forms of neoplastic growth, including malignant lesions. It covers much of the literature between 1900 and 1941, with data from about four thousand papers. Its value lies in the juxtaposition of the various lines of attack on the cancer problem, which is thus at least a start to clearing up misapprehensions; the practicing physician will find hints from the broad outlines of different familial types of susceptibility. Such may well be of use in the constant search for early diagnosis and ever earlier preventive treatment—the choice of therapeutic measures based on such a datum may also well be envisaged.

In this connection it is interesting to note the importance of comparison of the outlook on cancer with the data in the cross reference sections of the clearing house. Constitutional

This preliminary report was submitted and approved by the Council of the Bureau of Human Heredity in London and the Genetics Laboratory, Department of Zoology and Entomology, Ohio State University, under the joint auspices of which the survey of Constitution in Cancer was conducted.

traits are in many instances verifiable as genotypic or simple phenotypic. Thus a good deal that the specialist in cancer would view as speculative can be shown here to be factual from data so accumulated that they can be easily found.

One comment is permissible: The emphasis on mendelian formulas which dominates so much of the experimental work in genetics which has been surveyed will almost startle a reader conversant with papers of 1944. Now the interaction of gene with gene is coming increasingly to the fore, so that the picture of "modifiers," "degrees of penetrance" and so on, superimposed on the mendelian picture, has blurred the old outlines beyond recognition. The biologic-genetic entities, however, stand and to our thinking justify this modest attempt within the framework of the new "machine," the information center. The summarized genetic findings are not the less important for presenting no surprises.

The myth of hereditary cancer is disposed of. Geneticists are more and more aware in other fields of the fact that hereditary makeup controls type of constitution, in other words individual variations in physiologic function. Hence the statement in the early pages of this survey—"These and many other pedigrees and observations leave little doubt as to the importance of hereditarily determined factors" as precursors of the disease, as seen in localization of growth and type of neoplasm.

This may be stated in another way: Hereditary immunity, partial or complete, may be reckoned with, while proneness to benign and malignant tumors unquestionably exists.

Cancer Soil.—There is evidence from many sources that carcinogenic agents react differently on various types of constitution. This is the obverse of the foregoing statement and, again, would be expected by those versed in physiologic genetics. An illuminating point may be gleaned here, namely, that certain types respond quickly to diverse kinds of irradiation. Another type appears to be mainly due to hormonal imbalance, which prepares the body for benign and/or malignant tumors. Fortunately, data give at least a rough guide as to means of differentiating between the various types of the disease.

Other Diseases.—It is significant that certain hereditary diseases appear frequently as precursors of neoplastic growth and malignant lesions. Careful observation by physicians should soon add many facts under this heading. Here the clearing house may have special importance. Practitioners by contributing their observations to the center will do much to accelerate accumulation of knowledge of practical value for their colleagues and humanity.

The present opportunity for shared work with another organization fulfils our general aim of mutual worldwide activities and has given us in London the keenest satisfaction. We record our sense of gratitude to those who have turned this cherished dream into reality.

PRELIMINARY REPORT

Few subjects can present such a welter of complications, for research worker and physician alike, as that of tumors of man in relation to heredity. The groundwork has been covered in many apparently unrelated fields, and workers in botany, zoology, physics, chemistry, statistics and genetics have accomplished an enormous amount in their several lines. Their observations, however, appear in special journals, and the literature is scattered and not easily available, so that workers in one field are unlikely to be acquainted with results in others; while physicians, who have the best contact with actual cases and who could thus contribute highly valuable material, are frequently out of touch with research on the genetic aspects of cancer. Even when a physician has been led, through his observations on individual patients, to recognize the importance of hereditary factors in clinical histories, he is unable to follow them up readily, particularly in the case of cancer, because of the obstacles in the way of understanding the biologic complex that is involved. One cannot even guess how many valuable data may be lost for these reasons.

SURVEY OF CONSTITUTION IN CANCER

It was the aim, therefore, of the Survey of Constitution in Cancer: first, to collect the relevant data; then, to coordinate and cross index them according to the system followed by the Bureau of Human Heredity in its studies of genetic traits, and, further, to compare the validity of and collate the results in order to evaluate the real status of knowledge in this field and to examine and define areas demanding further exploration.

The accompanying form, devised to cover all the fields under survey, has proved satisfactory in handling the huge quantity of material examined, amounting to many thousands of separate references.

The work is by no means complete, nor indeed can it be ended while research in cancer continues. Nevertheless, at the stage now reached it is possible to present a preliminary summary of the role of genetics in cancer research, covering the period between 1900 and 1941. The object is not an exhaustive enumeration of the items but the coordination of developments and trends

in the several lines of inquiry, often seemingly remote from genetics, from the point of view of both genetics and the practice of medicine.

Work Sheet Used in Survey of Constitution in Cancer

No.

Author:

Title:

Reference:

Statistics	Man, Animals
Racial differences	Plants
Predisposition, general	
" localized	
" special types	
Cancer families	Spontaneous, induced, transplanted
Twins	Hereditary, acquired, indeterminate
Conjugal cancer	Cancerogenic agents
Congenital "	irritants
Multiple tumors	chemical
Cell processes	
chromosomal	mechanical
extrachromosomal	trauma
Age, sex	actinic rays
Body type, blood group	micro-organisms
Pigmentation	parasites
Endocrine system	
Blood-lymph "	
Nervous "	Occupational
Metabolism: body	Analysis:
" tumor	positive
Lactation	negative
Pregnancy	indeterminate
Fertility	
Developmental defects	Mode of transmission
Precancerous conditions	Extrachromosomal factors
Coexisting diseases	
Infection	Generalia
Lowered resistance	
Immunity	Bibliography
Environmental factors	

The selection and arrangement of material in the summary were necessarily limited by this purpose, and failure to mention the work of any author does not reflect on its importance in any way. The same fact accounts for the small number of references cited here out of the extensive collection in the archives of the Bureau of Human Heredity. Publication of the complete bibliography has been prevented by war conditions, but it and the final report on the survey will follow as soon as circumstances permit. In the meantime information about the material on file will be made available on request to interested students.

ROLE OF GENETICS IN CANCER RESEARCH

At the beginning of the twentieth century, research on cancer, which had hitherto been largely descriptive, entered on a wholly new phase, as a result of four factors: (1) the rediscovery of the laws of genetics; (2) the study of spontaneous and transplantable tumors in animals from the standpoint of heredity; (3) the study of cancerogenic agents, which opened the way for experimental study of induced tumors biologically controlled, with research on hormones an especially important section; (4) an increased knowledge of the biologic connection between irritants, and differences in individual reactions. How are these factors connected, and why is each one important for the study of the cancer problem?

Evidently no proper approach to the problem of cancer and heredity could be made and of course no solution could be found without knowledge of the principles governing hereditary transmission in general.

It was only in 1900 that these principles, the laws of genetics, which were discovered originally by the monk Gregor Mendel as early as 1866, were rediscovered by three investigators working independently of each other: Hugo de Vries, in Holland; Carl Correns, in Germany, and B. Tschermak, in Austria.

Since then a new branch of science has been developed, the importance of which cannot be better demonstrated than by giving facts about the role which genetics plays in modern cancer research. Indeed, the place of genetics in this particular field affords an excellent example of the value and aim of the study of heredity in general; certainly no serious discussion of the cancer problem could be carried out were the subject not included.

For the discovery of several nonspecific cancerogenic agents has not solved the problem; nor would the discovery of a prime causative agent, such as a bacillus or a virus, make everything clear. In either case the striking individual differences in susceptibility and immunity to malignant tumor growth would remain unexplained, as would the connection between such individual differences and variety or type of constitution.

But constitutional types in themselves cannot be easily defined or explained; nor is it easy to answer the apparently so simple question, "Is hereditary transmission involved as a major cause in a so-called cancer family?"

Evidence from several lines of approach may be consulted, of which at least five are considered in this review: statistics on cancer, histories of families, study of twins, experimentation on animals and response to cancerogenic agents.

I. STATISTICS ON CANCER

An unusually high incidence of cancer in a given family, or even in a number of families

within a community, does not of itself constitute statistical evidence for the heritability of cancer. For, by the law of probability, cancer is bound to occur with exceptional frequency in a certain number of families simply because of its high incidence in the general population, where it accounts for 1 out of every 10 deaths.

As early as 1913 Bashford estimated the number of deaths due to cancer that may occur in families of various sizes without warranting any assumption that hereditary factors are involved. The accompanying table, based on Bashford's

Probability of Multiple Cancer Cases Without Assuming Hereditary Tendency *

No. of Cancer Deaths in Family †	Per 100 Families of 6 Members, viz. 3 Men, 3 Women	Per 100 Families of 8 Members, viz. 4 Men, 4 Women	Per 100 Families of 10 Members, viz. 5 Men, 5 Women
None	47	36	28
One	38	39	38
Two	13	19	23
Three or more	2	6	11
	100	100	100

* After Bashford (1913-1914) as cited by Cramer.[1]
† All deaths before the age of 35 are excluded.

figures as cited by Cramer [1] in his paper on statistical investigations of cancer, published in 1937, indicates how frequently death may be expected to occur among families of six, eight and ten members surviving their thirty-fifth year. From this it is clear that a steady increase in the number of deaths due to cancer will occur with increasing size of a family, so that the proportion of families with no such deaths drops from 47 deaths in 100 families of six members, to 36 in 100 with eight members and to 28 in 100 families of ten members. The incidence of 1 death—38 or 39 per hundred families—is the same for the three sizes. But multiple deaths increase sharply, with the ratio of 2 deaths per family going from 13 to 19 to 23 families in 100; while 3 or more deaths from cancer may be expected in 2 out of 100 families with six members, in 6 of those with eight and in 11, or more than a tenth, of the families with ten members.

Thus, a high incidence of cancer in a single family means nothing so far as the problem of heredity and cancer is concerned unless the conditions are checked by careful statistical methods. But here one encounters difficulties even greater than those usually faced in examining hereditary traits in man, because the family histories of large groups are notably unreliable with regard to cancer. To lack of accurate knowledge about cancer among ancestors and mistakes of diagnosis not corrected by postmortem examination must be added the impossibility of surveying the histories of several generations in a given family. This is due to the fact that, in the main, cancer affects persons of advanced years and many die before reaching the age of greatest susceptibility, so that it is not possible to gather even meager bits of information that might be handed down from one generation to another. Finally, there is a psychologic handicap to such genetic research, due to the reluctance commonly felt about admitting death from cancer in one's own family.

To overcome these various obstacles special methods of statistical investigation had to be devised, of which one of the most skilful is that of Waaler [2]; as seen from his paper, Waaler's inquiry is also outstanding for the quantity and quality of the source material. The foundation for the study was the register of the Norwegian Cancer Committee, consisting of data collected over twenty-one years and covering the records of 6,000 patients from all parts of the country. The existence of cancer in families during three generations had to be determined, with special emphasis on its existence among the brothers and sisters of the patients. For control material, Waaler used all the data relating to spouses of patients. These data had the additional value of providing evidence on the influence of purely environmental conditions, including the possibility of infection for persons living under the same roof.

The questionnaire method proved wholly inadequate for gathering the precise information needed in such research. A corps of one hundred and fifteen medically trained helpers was distributed throughout the country, and the work went on for many months, till the mass of data required for this complicated statistical analysis was assembled. The results, published in 1931, cannot be summarized briefly, but some of the more generally applicable findings may be indicated by the following quotation from a paper by Weller [3]:

> As to spouses, he [Waaler] found that no excess cancer mortality over the general population existed. The incidence of cancer was significantly greater among the sisters of cancer patients than among the wives of the patients or in the general population. Among males, the difference was considered inconclusive. Waaler's figures show that the proportional cancer mortality in the siblings varies with cancer incidence in the parental generation. When one or the other parent had cancer, the proportions for male and female sibs were 40.7 and

1. Cramer, W.: The Importance of Statistical Investigations in the Campaign Against Cancer, Am. J. Cancer **29**:1-19, 1937.

2. Waaler, G. H. M.: Ueber die Erblichkeit des Krebses. Skrifter utgitt av det Norske Videnskaps-Akademie i Oslo: I. Mat.-Naturv. Klasse, 1931, no. 2.

3. Weller, C. V.: Intrinsic Factors in the Etiology of Neoplasms, Am. J. Cancer **30**:39-46, 1937.

53.8 per cent. When both parents died at ages over sixty years, of disease other than cancer, the corresponding figures were 21.7 and 23.1 per cent. The female sibs of patients with cancer of the breast, uterus, or ovaries showed a larger proportion of cancer than the male sibs, and the type of tumor from which the patient suffered was largely represented in her female sibs. For instance, cancer of the breast appeared in 44.7 per cent of the cancerous sibs of patients with cancer of the breast, and in but 16.5 per cent of the cancerous sibs of females with cancer other than of the breast. However, no such relationship was found to exist when the siblings of males with cancer of the lip were considered.

In an extensive review of Waaler's paper, Greenwood [4] pointed out:

> Waaler's findings are consistent with, although they do not prove (as Waaler rightly says), the truth of an hypothesis of the following type:
>
> (1) That some forms of cancer (e. g. lip cancer) are produced quite independently of any inheritable anlagen, and that extrinsic factors have greater, perhaps exclusive influence upon males.
>
> (2) Second, that the heritable factors are two independent factors, both of which occur with a frequency of about 16 per cent.

Wassink [5] made a similarly thorough investigation in the Netherlands, obtaining results greatly like those of Waaler. One of the most important observations in both studies was the striking difference in behavior of tumors of different localization.

The existence of a pronounced hereditary tendency to mammary cancer has also been demonstrated by the Russian investigator Martynova,[6] who, in an elaborate study of 201 family histories, found that cancer of the breast is not only more frequent in all female relatives of patients suffering from mammary cancer but eighteen times as frequent in the mothers of patients with cancer of the breast as in mothers of similar age among the control population.

The complexity of the problem can be easily realized from these quotations, although they convey but a weak impression of the vast extent of the labors of investigators in this field. One of the most significant conclusions emerging from these admirable studies is that cancer is not a unit disease, because tumor growths of different sites and types behave genetically in different ways.

This fact emphasizes clearly the necessity for recording and investigating data on the incidence of cancer in man separately for each tissue and organ.

4. Waaler,[2] abstracted, Cancer Rev. **7**:464-470, 1932.

5. Wassink, W. F.: Cancer et hérédité, Genetica **17**:103-144, 1935.

6. Martynova, R. P.: Studies in the Genetics of Human Neoplasms: Cancer of the Breast, Based upon 201 Family Histories, Am. J. Cancer **29**:530-540, 1937.

II. FAMILIES WITH CANCER

From time to time in medical literature families are described who show not only an extremely high incidence of cancer among their members but a similar and sometimes unusually early onset of the disease and localization in the same or homologous organs. One well known and much cited pedigree, that of "family G.," was first reported by Warthin [7] in 1913, who presented a further study twelve years later.[8] In 1936, Hauser and Weller [9] brought the record of Warthin's "cancer family" up to date and gave the following figures with regard to the incidence and the site of tumors in this history: Up to 1936 there have been observed "43 primary carcinomas in 41 individuals from a total population of 305. Since only 174 have attained the age of twenty-five years, this gives the high cancer incidence of not less than 23.6 per cent in those reaching that age.

But Hauser and Weller rightly found the anatomic location of the primary lesions even more significant than the high incidence of cancer in this family, with 26 of the 43 carcinomas having occurred in the gastrointestinal tract and 15 in the endometrium. Of the carcinomas, 20 occurred in males, all of them in the gastrointestinal tract. Since not a single example of cancer in other organs occurred among these persons, pure chance cannot account for this unique distribution.

Interest in the study of such family histories far antedates the modern science of genetics. Long before the discovery of Mendel's laws, the attention of laymen and physicians was drawn to the occasional high incidence of cancer, especially when it concerned a famous family, like that of Napoleon Bonaparte, who died of cancer of the stomach, while three sisters, one brother, his father and his grandfather are all supposed to have died from gastric carcinoma. The pedigree, as published recently by Sokoloff,[10] may be mentioned because of its historical interest.

In 1856, two famous physicians, Broca and his father-in-law, Lugol, recorded information on a family (probably their own) which included three medical men. Wolff [11] published their

7. Warthin, A. S.: Heredity with Reference to Carcinoma, Arch. Int. Med. **12**:546-555 (Nov.) 1913.

8. Warthin, A. S.: The Further Study of a Cancer Family, J. Cancer Research **9**:279-286, 1925.

9. Hauser, I. J., and Weller, C. V.: A Further Report on the Cancer Family of Warthin, Am. J. Cancer **27**:434-449, 1936.

10. Sokoloff, B.: Predisposition to Cancer in the Bonaparte Family, Am. J. Surg. **40**:673-678, 1938.

11. Wolff, J.: Die Lehre von der Krebskrankheit, Jena, G. Fischer, 1907, vol. 1, p. 363 (cites report on family by Broca and Lugol in 1856).

figures in 1907, and again here is evidence of specific organ susceptibility since among the total of 16 cases of cancer 10 were instances of cancer of the breast and 4 of cancer of the liver.

A more recent example, reported in 1932 by Finney,[12] was the family in which 8 members—a mother, 4 daughters and 3 nieces—had all been operated on for cancer at the Mayo Clinic. All but 1 of these patients had cancer of the breast; 3 of the daughters had a second cancer in the other breast, and 1 of these 3 later had cancer of the stomach.

More than a hundred such families have been reported in medical literature. The record most important for this study is that of a type of tumor so rare that the probability of its chance occurrence more than once within the same family is extremely small. For example, Macklin[13] noted that among the 60 cases of retinal angioma (the total recorded up to 1930) 6 cases were in one family and there were two families with 3 cases each.

These and many other pedigrees and observations of the kind leave little doubt as to the importance of hereditarily determined factors in formation of tumors, especially in the localization of certain forms.

III. THE STUDY OF TWINS

The same conclusions about the hereditary factors in the genesis of cancer follow the now classic method of studies and observations on twins. In 1940, von Verschuer and Kober[14] surveyed the material so far published on the incidence of cancer among twins, giving data for 48 pairs of identical and 61 pairs of fraternal twins in which tumors occurred in 1 or both partners, taking into account localization of the disease in each case. Because the authors were dissatisfied with the way in which the material had been assembled, expressing the opinion that it could not yield conclusive statistical evidence on analysis, since it was made up largely of selected cases or series of cases, they added a preliminary report on their own unselected series of 23 pairs of identical and 56 pairs of fraternal twins.

From their analysis of this extended series (188 pairs in all) von Verschuer and Kober decided that so far there was no proof of the existence of a general hereditary predisposition to cancer, although they confirmed earlier findings of definite hereditary factors with respect to the localization of the disease.

Similar conclusions had been reached by Kranz in 1932[15] from his analysis of 22 cases and by Versluys in 1934[16] from his 27 cases of tumor in twins.

The factor for localization is especially prominent in cases of cancer of the stomach, in which, as von Verschuer and Kober pointed out, the behavior of the disease differs in identical and nonidentical twins, while no significant differences were observed in the behavior of mammary cancer in identical as compared with fraternal twins.

The number of cases of cancer in twins which has been investigated is still far too small to yield conclusive evidence; indeed, this is only the beginning, and a considerable amount of material must be gathered and studied before statistically valid results can be obtained in this important and promising field of research.

IV. EXPERIMENTS ON ANIMALS

While the carefully devised methods of human genetics, as used in the study of data on population and family histories or in observations on twins, may help to arrive at some conclusions about the problem of hereditary factors in cancer, they cannot solve it because of difficulties inherent in the nature of the subject matter. To clarify certain fundamental issues experimentation on animals must be employed, whereby it is possible to survey rapidly a number of generations of individuals, watched under controlled conditions and bred appropriately.

Work in this field started with observations on and experiments with spontaneous and transplanted tumors in rodents, especially mice. From among the many workers with whose names this line of research is identified, the following are mentioned, according to the approximate sequence in which their results were presented: Jensen, Borrell, Ehrlich, Apolant, Bashford, Murray, Haaland, Loeb, Cramer, Murphy, Tyzzer, Slye, Little, Strong, Bittner, Lynch and Dobrovolskaja-Zavadskaja.

A. The Mode of Transmission.—Four major problems were met by those undertaking a study of the behavior of tumors in animals, and the

12. Finney, W. P.: A Cancer Family, Proc. Staff Meet., Mayo Clin. **7**:383-384, 1932.

13. Macklin, M. T.: Heredity in Cancer and Its Value as an Aid in Early Diagnosis, Edinburgh M. J. **42**:49-67, 1935.

14. von Verschuer, O., and Kober, E.: Die Frage der erblichen Disposition zum Krebs, Ztschr. f. Krebsforsch. **50**:5-14, 1940.

15. Kranz, H.: Tumoren bei Zwillingen, Ztschr. f. indukt. Abstammungs- u. Vererbungsl. **62**:173-181, 1932.

16. Versluys, J. J.: Zwillingspathologischer Beitrag zur Aetiologie der Tumoren, Ztschr. f. Krebsforsch. **41**: 239-259, 1934.

literature has centered mainly about the questions of whether there is or is not: (1) a species difference in susceptibility or refractoriness to formation of tumor; (2) an inheritable general predisposition or refractoriness to formation of tumor; (3) an inheritable proneness to specific types of tumor or to specific localization of the disease. And if these queries are to be answered in the affirmative, there remains a fourth question: What is the mode of transmission of the hereditary traits involved, expressed in mendelian terms?

Various methods have been developed by different investigators, according to their ideas of how these questions might best be answered. The amount of work accomplished in this line is enormous, defying a short survey. But in spite of widely different opinions about the proper procedure, certain highly important observations have been verified and finally established as facts by the brilliant and tireless work of many investigators, and there is now general agreement on the answers to the first three questions:

1. Species difference: Cancer is a disease affecting all species of vertebrates, but different species behave differently in general susceptibility to formation of tumor as well as in predisposition to specific types of tumor and to specific localization.

2. General predisposition: There is likewise an undoubtedly different behavior in general susceptibility or refractoriness to formation of tumor among mice of genetically different strains.

3. Localization: Further, there are inheritable factors for specific types and specific localization of tumors. Such genetically determined differences are especially distinct in susceptibility or refractoriness to mammary cancer in mice, which is the most thoroughly investigated form of the disease.

Cancer of the breast, for example, has been found to occur spontaneously in a large percentage and can be developed by appropriate breeding methods in over 90 per cent of the mice of certain strains, known as high cancer strains, while in other strains it hardly occurs at all and cannot be induced artificially, so that the figure for mammary cancer remains practically zero in the low cancer strains.

By appropriate crossing of high and low cancer strains, the percentage of mammary cancer in the progeny can be varied almost at will.

4. Mendelian mechanism: Although these important basic facts have been established to the general satisfaction of the investigators, there is still much divergence of opinion as to the mendelian mechanism that is involved in the transmission of the traits.

The question as to whether susceptibility and refractoriness to formation of tumors are dependent on multiple factors or whether they are unit characters and, furthermore, whether they are dominant or recessive has precipitated a long controversy in genetic literature; the discussion has been heated at times.

One of the prominent workers in the field, Slye,[17] after many years of observation on the genetic behavior of cancer of the breast in mice, involving many generations and many thousands of individual records and autopsies, arrived at two conclusions: First, the genetic difference between susceptibility and insusceptibility to cancer involves one gene; that is, they are unit characters; second, in the stock of her laboratory, susceptibility to cancer behaves like a recessive; while insusceptibility behaves like a dominant character.

Little[18] and other investigators have, with apparently good reason, contradicted Slye's conclusions. In the course of the discussion, Bernstein compared her findings with the protocols of the experiments performed by Loeb and Lathrop, and in his statistical analysis he was able to reconcile seemingly contradictory observations in the two investigations, purely on the basis of statistical reasons.

Bernstein[19] finally reported in 1930 that he was inclined to assume that Slye's viewpoint was correct as to the recessive character of susceptibility to mammary cancer in mice.

But with much evidence amassed in the years immediately following Bernstein's analysis, it now appears obvious that the mode by which mammary cancer is transmitted is not nearly so simple as that.

B. Extrachromosomal Factors and the Milk Factor.—Even yet it remains to be determined whether transmission follows strictly mendelian laws, since recent observations by Little and other members of the staff of the Roscoe B. Jackson Memorial Laboratory[20] and indepen-

17. Slye, M.: Studies in the Incidence and Inheritability of Spontaneous Tumors in Mice (a series of reports, the first of which appeared in Ztschr. f. Krebsforsch. **13**:500-504, 1913, and the next in J. M. Research **30**:281-298, 1914, where the series was continued for some years, after which it was continued in the *Journal of Cancer Research*).

18. Little, C. C.: Evidence that Cancer Is Not a Simple Mendelian Recessive, J. Cancer Research **12**: 30-46, 1928.

19. Bernstein, F.: Ueber die Erblichkeit und Natur des Krebses, Med. Klin. **26**:1583-1587 and 1621-1625, 1930.

20. Little, C. C.: The Existence of Non-Chromosomal Influence in the Incidence of Mammary Tumors in Mice, Science **78**:465-466, 1933.

dently by Korteweg [21] in Amsterdam have demonstrated that development of cancer of the breast in mice may depend largely on cytoplasmic or extrachromosomal factors.

In addition, it was shown by Little and Bittner [22] and subsequently confirmed by other investigators that the influences of foster nursing, the so-called milk factor, are also operative. Mice nursed by mothers of a high cancer strain show a significantly higher incidence of mammary cancer than litters nursed by mothers of a low cancer strain, and vice versa; while nursing has little or no bearing on the development of primary pulmonary carcinoma.

These are obviously most important findings, the implications of which in the development of cancer are now under thorough investigation.

However, with these questions still unsettled, even in experimentation on animals, it is obviously too early to try to make definite statements about the mode of transmission that may be involved, that is, whether through unit characters, dominant or recessive, or through cytoplasmic influences or to try to relate these findings, translated into mendelian terms, to the far more difficult problem of cancer in a human being.

But, one may ask, what practical value results from such genetical work with animals? Can it show anything tangible, increasing understanding of human cancer?

The answer is that work in animal genetics has shown with some approximation to certainty that heredity does play a part in certain forms of the disease and further that the hereditary factors are not of equal significance and that they differ according to the type and site of the tumor. These facts mean that cancer cannot be regarded as an entity in its genetic aspects, a definite if negative conclusion, which will be useful in guiding further inquiry. Again, it has been learned, in part through experimentation on animals, that hereditary factors must not be given undue weight or regarded as the sole conditioning elements in growth of cancer but that other influences have a part.

V. CANCEROGENIC AGENTS

By a fortunate coincidence, just about the time knowledge in the genetic field of cancer research had been enormously widened, important developments in apparently unrelated fields made possible an increasingly successful study on the relation between external and constitutional factors in the growth of tumors. About thirty years ago several independent investigators found that cancer could be induced in the tissues of animals by application of various agents, including certain parasites, viruses and chemical compounds.

A. Parasites.—In 1913, Fibiger in Copenhagen [23] stated that cancer of the forestomach of the rat could be induced by infection with the parasite Gonglyonema neoplasticum.

B. Virus.—Rous [24] in 1911 first described a transplantable sarcoma in a chicken, produced by the injection of a cell-free extract, supposedly a virus, into a normal fowl; after this much work with viruses was done, by Rous, Gye and others.

The observations of Fibiger and Rous offer many important leads in search for a possible prime causative agent in formation of cancer. But it has not yet been demonstrated convincingly that either a parasite [25] or a virus is such a prime agent, whether in rodents or in man, while in both organisms cancer may be produced more readily by the different means of chemical compounds.

C. Chemical Compounds.—It has long been observed that some substances in soot and tar must have cancerogenic properties; so-called occupational cancers, such as "chimney sweep" cancer and cancer of the skin among workers coming in contact with tar, especially that originating from gas works, were well known and often described in medical literature of the last century.

The possibility of inducing cancer by chemical means was first demonstrated in 1915 by two Japanese workers, Yamagawa and Ichikawa,[26a] who found that they could do this by continuously painting the skin on rabbits with tar, whereas Tsutsui [26b] in 1918 succeeded in obtain-

21. Korteweg, R.: Chromosomale invloeden op den groei en extra-chromosomale invloeden op het onstaan van kanker bij de muis, Nederl. tijdschr. v. geneesk. **79**:1482-1490, 1935.

22. Bittner, J. J., and Little, C. C.: The Transmission of Breast and Lung Cancer in Mice, J. Hered. **28**:117-121, 1937. Bittner, J. J.: Relation of Nursing to the Extrachromosomal Theory of Breast Cancer in Mice, Am. J. Cancer **35**:90-97, 1939.

23. Fibiger, J.: Untersuchung über eine Nematode (*Spiroptera* sp. n.) und deren Fähigkeit, papillomatöse und carcinomatöse Geschwulstbildungen im Magen der Ratte hervorzurufen, Ztschr. f. Krebsforsch. **13**:217-280, 1913.

24. Rous, P.: Sarcoma of the Fowl Transmissible by an Agent Separable from the Tumour Cells, J. Exper. Med. **13**:397-411, 1911.

25. Fibiger's work on the rat is now, in view of the research work of Passey, Bullock and Rhodenburg, Cramer and others, considered of doubtful value.

26. (*a*) Yamagawa, K., and Ichikawa, K.: Experimentelle Studie über die Pathogenese der Epithelialgeschwülste, Mitt. a. d. med. Fakult. d. k. Univ. zu Tokyo **15**:295-344, 1915-1916. (*b*) Tsutsui, H.: Ueber das künstlich erzeugte Cancroid bei der Maus, Gann **12**: 17-21, 1918.

ing similar results in mice. Shortly thereafter, Bloch and Dreyfuss, in Switzerland, were able to determine that this cancerogenic action was due to neutral, nitrogen-free substances with a high boiling point.[27]

The next most outstanding event occurred when the spectrographic observations of Hieger and Mayneord led a group of British workers to the discovery of a series of pure hydrocarbons with strong cancerogenic properties.[28] A characteristic common to these compounds is a phenanthrene group of benzene rings, similar to the substances known as sterols, which occur in normal metabolism of both plants and animals.

A further striking observation was made when, largely through the work of Doisy and co-workers[29] and of Butenandt,[30] the chemical constitution of the estrogenic substances in the urine of pregnant women was shown to be like that of the most active cancerogenic compound: 1, 2, 5, 6-dibenzanthracene.[31]

The importance of these discoveries, which followed each other in rapid succession, can hardly be overestimated, for with them it was possible to induce tumors in animals by means of chemical agents, the exact chemical structure of which was known and the cancerogenic properties of which could be controlled. Knowledge of these substances enables one to understand how cancer may develop locally, as, for example, in the skin when it is brought into close contact with them for a long enough time. Moreover, the close chemical relationship between these substances and certain physiologic products of the body gives a clue to the understanding of how, under certain abnormal conditions, a deranged metabolism or the endocrine system may play a part in the development of cancer in organs remote from any external irritation, by providing what Cramer called a favorable "internal cancerogenic environment."

VI. INTERNAL CANCEROGENIC ENVIRONMENT IN EXPERIMENTAL ANIMALS

A. Hormones.—A relation between the endocrine system and some forms of tumor growth has been recognized since 1916, when Loeb and Lathrop[32] made their classic observations on the influence of oophorectomy on the incidence and age at onset of mammary carcinoma in mice. However, while this discovery long antedated those just enumerated in the field of chemistry, the latter have enormously enlarged the understanding of the whole matter.

Investigations by Loeb and his co-workers and Cramer, Andervont, Lacassagne and others have brought to light a mass of facts which definitely shows the importance of the endocrine system and especially of estrogens in the development of mammary cancer. Thus a few years ago, Lacassagne,[33] in his experiments in Paris, was able not only to increase the incidence of mammary cancer in female mice by means of long-continued injections of estrogen but to show that cancer of the breast can be made to develop under the conditions of his experiment in 100 per cent of male mice in which mammary cancer normally did not appear spontaneously.

But here again the most striking differences in reaction could not be explained without the knowledge gained by research in the genetic field. Lacassagne, working with various inbred strains of mice of known genetic susceptibility or refractoriness to cancer, achieved results which varied consistently with the strain, in respect both to the degree to which mammary cancer might be induced by injections of estrogen and to the age at which it was produced. His findings may be summarized from Cramer's report

27. Bloch, B., and Dreyfuss, W.: Ueber die experimentelle Erzeugung von Carcinomen mit Lymphdrüsen- und Lungenmetastasen durch Teerbestandteile, Schweiz. med. Wchnschr. **2**:1033-1037, 1921.

28. Kennaway, E. L.: The Formation of a Cancer Producing Substance from Isoprene (2-Methyl-Butadiene), J. Path. & Bact. **27**:233-238, 1924. Cook, J. W.; Hieger, I.; Kennaway, E. L., and Mayneord, W. V.: The Production of Cancer by Pure Hydrocarbons: I., Proc. Roy. Soc., London, s. B **111**:455-484, 1932. Cook, J. W.: The Production of Cancer by Pure Hydrocarbons: II., ibid. **111**:485-496, 1932. Cook, J. W.; Haslewood, G. A. D.; Hewett, C. L.; Hieger, I.; Kennaway, E. L., and Mayneord, W. V.: Chemical Compounds as Carcinogenic Agents, Am. J. Cancer **29**:219-259, 1937. Cook, J. W., and Kennaway, E. L.: Chemical Compounds as Carcinogenic Agents, ibid. **33**: 50-97, 1938; **39**:381-428 and 521-582, 1940.

29. (*a*) Doisy, E. A.; Thayer, S., and Veler, C. D.: The Preparation of Crystalline Ovarian Hormone from the Urine of Pregnant Women, J. Biol. Chem. **86**:499-509, 1930. (*b*) Veler, C. D.; Thayer, S., and Doisy, E. A.: The Preparation of the Crystalline Follicular Ovarian Hormone: Theelin, ibid. **87**:357-371, 1930.

30. Butenandt, A.: Ueber "Progynon." ein krystallisiertes weibliches Sexualhormon, Naturwissenschaften **17**:879, 1929.

31. Domagk, G.: Die synthetisch hergestellten carcinogenen Substanzen und ihre Beziehungen zu physiologischen Produkten, Ztschr. f. Krebsforsch. **44**:160-186, 1936.

32. Lathrop, A. E. C., and Loeb, L.: Further Investigations on the Origin of Tumors in Mice: III. On the Part Played by Internal Secretion in the Spontaneous Development of Tumors, J. Cancer Research **1**:1-19, 1916. Loeb, L.: Further Investigations on the Origin of Tumors in Mice: VI. Internal Secretion as a Factor in the Origin of Tumors, J. M. Research **40**:477-496, 1919.

33. Lacassagne, A.: Influence d'un facteur familial dans la production, par la folliculine, de cancers mammaires chez la souris mâlé, Compt. rend. Soc. de biol. **114**:427-429, 1933.

on etiology of cancer of the mamma,[34] as follows:

1. Cancer of the breast in inbred strains of mice with a high spontaneous incidence of mammary cancer (72 per cent) could be developed in all male and female mice by treatments with estrogen, with tumors appearing at an early age (4 to 10 months).

2. In a strain with a low percentage (2 per cent) of spontaneous mammary cancer in female mice, mammary cancer appeared after applications of estrogen to both males and females, but only at a late age (9 to 18 months).

3. In a strain in which cancer of the breast did not appear spontaneously in many generations of females, mammary cancer could not be induced in either sex, even if the mice received injections of large quantities of estrogen continuously from birth to maturity.

The bearing which genetically determined factors have on the development and the age at onset of mammary cancer can hardly be demonstrated more convincingly. Lacassagne suggested that the hereditary factor consists of an unequal response of the mamma to the same quantity of hormone. But what is the nature of the hereditary factors which determine such striking differences in the response of the mamma to estrogen?

B. Endocrine Abnormalities.—Recent observations may bring nearer an answer to this question. Cramer and Horning [35] have demonstrated that in the RIII strain of mice a high incidence of spontaneous mammary cancer is always associated with a visible pathologic process, known as "brown degeneration," in certain parts of the adrenals, which precedes the onset of mammary cancer. This process seems to be specific for this high cancer strain and has never been seen in the adrenals of mice of the ordinary mixed strain, more than 1,000 of which were examined by the investigators during fifteen years.

Cramer and Horning stated the belief that they have evidence that this pathologic condition may be related to the breakdown of a restraining mechanism which normally antagonizes the carcinogenic action of estrogen on the mamma. A close relation between the action of estrogen, the adrenal glands and the specific susceptibility of the high cancer RIII strain to estrogenic action seems to be proved by the the following fact:

If mice of the RIII strain in which "brown degeneration" sets in spontaneously are treated with estrogen, the adrenals of these mice undergo a much quicker and more extensive process of "brown degeneration" than the adrenals of mice with a low incidence of cancer.

34. Cramer, W.: On Aetiology of Cancer of the Mamma in the Mouse and in Man, Am. J. Cancer **30**: 318-331, 1937.

35. Cramer, W., and Horning, E. S.: Adrenal Changes Associated with Oestrin Administration and Mammary Cancer, J. Path. & Bact. **44**:633-642, 1937. On the Association Between Brown Degeneration of the Adrenals and the Incidence of Mammary Cancer in Inbred Strains of Mice, Am. J. Cancer **37**:343-354, 1939; Hormonal Relationship Between the Ovary and the Adrenal Gland and Its Significance in the Aetiology of Mammary Cancer, Lancet **1**:192-197, 1939.

VII. INHERITED LOCALIZATION FACTOR IN MAN

The implication of the findings of Cramer and Horning for the experiments of Lacassagne, and most probably for the whole problem of mammary cancer, is clear. In addition they hint at the possibility that at least the localization factor in certain cases of tumor formation may be explained by abnormal endocrine conditions. These factors may be inherited independently of general susceptibility to formation of tumor, as Bernstein pointed out in the investigations referred to earlier.[19]

A. Endocrine Traits.—Bernstein explained that from the protocols of experiments on animals used in his analysis, the problem of whether localization of cancer is determined by factors dependent on general susceptibility was not solved. He expressed the opinion that the factors conditioning localization were not dependent on general susceptibility.

According to Cramer and Horning's observations, a localization factor in mice may be found in an inherited abnormal endocrine trait and most likely in other inborn conditions and the study of these conditions is of the greatest importance to the question of cancer in human beings.

My own investigations, conducted at the Genetics Laboratory of Ohio State University in cooperation with the Columbus Cancer Clinic and the University General Hospital, point in this direction. For example, there is some reason to believe that certain abnormalities in the whole range of the menstrual cycle may give a clue to better understanding of why mammary cancer runs in some families.

A positive relationship between delayed menopause and carcinoma of the breast and of the body of the uterus has already been suggested by some authors. Thus, in 1937 Olch,[36] after investigating the age at menopause among women suffering from mammary cancer, reported his conclusion that the number of patients in this group who continued to menstruate after the age of 50 was nearly five times as high as might be expected.

36. Olch, I. Y.: The Menopausal Age in Women with Cancer of the Breast, Am. J. Cancer **30**:563-566, 1937.

I have checked Olch's figures by comparing them with the recorded ages at menopause among two other groups of women: first, those suffering with cancer of other sites than the breast or genital tissues and, second, patients treated in a general hospital for definitely noncancerous condition. Although, according to the findings of this investigation,[37] the differences between cancerous and noncancerous conditions with respect to age at menopause are not nearly so great as Olch assumes, they are sufficient to deserve more thorough investigation. But in my opinion one must take into consideration not only the age at menopause but the age at onset of menstruation as well, in order to determine the length of time the tissues have been subjected to estrogenic action. This approach would seem the more logical in view of the fact that (in temperate climates at least) the earlier the age at puberty the later the age at menopause; the reverse also holds, that the later the onset the earlier the cessation of menstruation.

Consequently, wide variations in the range of the cycle are bound to occur, so that it covers a relatively long period in the life of some women and a relatively short span in others. With our expanding knowledge of estrogenic action it seems worth while to study these variations more closely, particularly as there seems to be definite support for the belief that the range of the menstrual cycle is hereditarily determined, as suggested by many experienced physicians and by some geneticists.

Aside from the admittedly great influence of environmental factors, there is strong evidence to support the view that at least the time of onset of menstruation is hereditary. Comparing monozygotic and dizygotic twins, Petri [38] found an average difference of only two and eight-tenths months in the time of onset of menstruation in identical twins, but as much as twelve months in fraternal twins. Without going into further details or anticipating the results of my own investigations, it may be said that the assumption is justified that hereditary factors are operative in determining the range of the menstrual cycle.

The question concerned here is whether or not there is an unusually high incidence of cancer of the breast in the female members of families in whom early onset and late ending of the cycle occur or, in other words, in whom unduly prolonged estrogenic activity may create a "favorable cancerogenic internal environment."

37. Blank, F.: Late Menopause and Cancer of the Breast, Ohio J. Sc. **44**:51-56, 1944.

38. Petri, E.: Untersuchungen zur Erbbedingtheit der Menarche, Ztschr. f. Morphol. u. Anthropol. **33**: 43-48, 1934.

Cramer, in one of his recent brilliant papers on mammary cancer,[39] remarked that the existence of an inherited internal cancerogenic environment was of the greatest importance for the genesis of mammary cancer in man. And, pointing out that "there are definite indications that this internal carcinogenic environment may be related to endocrine abnormalities," he urged that investigations be made on man in this important matter. Regrettably, his advice has not yet been met with the response it deserves, for here is a wide open field for much needed research.

B. Inherited Precancerous Conditions.—Besides endocrine disturbances there are other conditions favoring the development of an internal cancerogenic environment, which further are known in many instances to have a genetic background. For example, von Verschuer and Kober [14] found evidence in their material about twins of a relation between the familial type of achlorhydria and the incidence of gastric cancer, which others noted in a study of family histories.

The true nature of some of the so-called precancerous conditions is not known, though their hereditary character is beyond doubt; for example, neurofibromatosis and tuberous sclerosis, or epiloia, appear as family traits and lead frequently to formation of cancer. Intestinal polyposis has been established, notably through the work of Lockhart-Mummery,[40] Dukes [41] and Jüngling,[42] as a frequent basis for the development of malignant growths in members of families affected by this condition.

Xeroderma pigmentosum offers an example of the role heredity plays in interaction with purely external factors. As is known, this condition, which is transmitted as an incomplete sex-linked recessive, invariably leads to formation of cancer in the skin of all the members of a family who have inherited the disease. There is reason to believe that xeroderma pigmentosum is connected with an inherited abnormality in metabolism, leading to development of photosensitive substances in the body similar to those found in hematoporphyrinuria.

C. Inherited Metabolic Abnormalities.—According to Joannovics,[43] it was noted by

39. Cramer, W.: On Aetiology of Cancer of the Mamma in the Mouse and in Man, Am. J. Cancer **30**: 318-331, 1937.

40. Lockhart-Mummery, J. P.: Cancer and Heredity, Lancet **1**:427-429, 1925.

41. Dukes, C.: The Hereditary Factor in Polyposis Intestini, or Multiple Adenomata, Cancer Rev. **5**:241-256, 1930.

42. Jüngling, O.: Polyposis intestini: Hereditäre Verhältnisse und Beziehungen zum Carcinom, Beitr. z. klin. Chir. **143**:476-483, 1928.

43. Joannovics, G.: Experimentelle Studien zur Geschwulstdisposition, München. med. Wchnschr. **63**: 575-576, 1916.

Kosanowics that hematoporphyrinuria was present in 14 cases of malignant tumor in regions subjected to the action of sun rays, although it was absent in cases of carcinoma in which the growth was in regions not so subjected. Moreover, Fischer-Wasels [44] stated that the condition in such cases was due to a constitutional anomaly caused by the reaction to light. And, in his paper on the influence of photosensitizing substances, Buengler [45] expressed agreement with Fischer-Wasels that the known hypersensitivity of the skin in xeroderma pigmentosum can therefore be regarded as simply a more severe degree of the same constitutional abnormality.

Roffo [46] observed an increase of cholesterol content in areas of the skin subjected to actinic rays, coinciding with the development of cutaneous cancer. Further research is needed to determine whether this is a reaction normally occurring under the influence of actinic rays or whether it reflects a constitutional tendency to some anomaly in cholesterol metabolism.

VIII. RACIAL DIFFERENCES IN INCIDENCE OF CANCER

Differences among various racial groups in the incidence of certain forms of cancer have been reported by a number of observers, notably in connection with the distribution of cancer of the skin and tumors of the stomach and the liver.

A. Cancer of the Skin.—Roffo,[47] in further studies of the role of actinic rays in the development of cancer of the skin, pointed out certain differences in reaction which are definitely constitutional or racial. He noted that in general sufferers from epithelioma have white, extremely photosensitive skins, while he has never found a single instance of this condition among Negroes or mulattos or in the native population of such countries as Argentina, though he has examined large numbers of cases.

Findlay,[48] in an important paper on ultraviolet rays and cancer of the skin, made a similar comment eight years before Roffo and cited Hyde's findings in an American study in 1906 to the effect that "the colored races suffer much less from skin cancer than the whites, among whom cancer of the face, neck and hands is especially common in agricultural laborers." Findlay referred also to the work of Corlett (1915) and McCoy (1920), who considered pigmentation of importance in the genesis of cancer of the skin. In McCoy's series of cases, the distribution of cancer of the face, neck and hands differed according to the type of pigmentation, as follows: 62 per cent in blondes; 31 per cent in *châtains* (those with dark hair but with little cutaneous pigmentation), and 7 per cent among dark-skinned persons.

Findlay further quoted from Molesworth's study in Australia (1927):

> ". . . rodent ulcer and epithelioma both develop in relation to pre-existing keratosis, more especially when the skin is poorly pigmented. Since those of Scottish and Irish descent have as a rule fair skins, the incidence of skin cancer of the face, hands and neck is far greater in these races than among the general population, while among Italians, on the other hand, skin cancer is very rarely seen."

B. Cancer of Internal Organs.—Although these conditions undoubtedly point to some genetical influences, it is also evident that environmental factors—such as climate, nutrition, occupation or clothing—are important and may indeed largely account for the differences in site incidence, not alone in cancer of the skin but in that of internal organs.

Clearly, only the most discriminating investigation into all the possible factors, internal and external, can be of value in discovering what are the purely racial influences in the differential incidence of tumor growth in various populations. Such research has already led to important results and the assembly of a vast amount of comparative data from all parts of the world. I can only mention in passing the now classic statistical inquiries of Hoffmann, notably those among the Indians of North and South America and the investigations conducted by Niceforo and Pittard,[49] under the auspices of the Section on Hygiene of the League of Nations. The most fruitful studies of race and cancer are those made in the Far East, with its peculiarly favorable conditions for this kind of inquiry.

In 1935, Bonne [50] reported on certain outstanding differences in the site incidence of cancer as it affected native Malay as compared

44. Fischer-Wasels, B., in Bethe, A.; von Bergmann, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1927, vol. 14, pt. 2, p. 1560.

45. Buengler, W.: Ueber den Einfluss photosensibilisierender Substanzen auf die Entstehung von Hautgeschwülsten, Ztschr. f. Krebsforsch. **46**:130-166, 1937.

46. Roffo, A. H.: Insorgenza di tumori maligni da irradiazione solare totale, Pathologica **27**:443-461, 1935.

47. Roffo, A. H.: Role of Ultraviolet Rays in the Development of Cancer Provoked by the Sun, Lancet **1**:472-474, 1936.

48. Findlay, G. M.: Ultraviolet Light in Skin Cancer, Lancet **2**:1070-1073, 1928.

49. Niceforo, A., and Pittard, E.: Considérations sur les rapports présumés entre le cancer et la race, d'après l'étude de statistiques anthropologiques et médicales de quelques pays d'Europe, Publ. de la Soc. des Nations: III. Hygiene, Geneva, World Peace Foundation, 1926.

50. Bonne, C.: Cancer in Java and Sumatra, Am. J. Cancer **25**:811-821, 1935; Cancer and Human Races, ibid. **30**:435-454, 1937.

with Chinese populations in Java which confirmed similar observations made in 1923 by Snijders and Straub [51] about Malay and Chinese laborers in the island of Sumatra.

Bonne found that there is a nearly total absence of gastric cancer among the native Malay population of Java, associated with a similar scarcity of gastric ulcer, though the Chinese in Java and in the tropical parts of the Far East generally have the usual amount of gastric carcinoma and gastric ulcer. It is impossible at present, Bonne explained, to say whether the prevalence or scarcity of gastric carcinoma depends on genetic factors or on external factors of irritation or on both of these. Without raising the question of the nature of the relationship between gastric ulcer and gastric cancer, the peculiar behavior of these two conditions among the native populations of Java and Sumatra suggests that both may be related to a basic factor of etiologic importance. This may prove to be either an inborn racial character or something in the living habits of the Malays, for example their food. All that can now be said, Bonne went on to state, is that rarity of gastric carcinoma appears to be a special characteristic of the nearly 40,000,000 native inhabitants of Java, a fact well worthy of further close study.

Primary liver cell cancer, a form rare in Europe, is of frequent occurrence in the Far East, usually developing in a cirrhotic liver of the Laennec type. This was noted by Bonne in Java and by Snijders and Straub in Sumatra; there are other reports on a similar prevalence of cancer of the liver in certain populations of Africa, including the Bantus and the natives of Cameroon and Nigeria as well as the natives of Northern India. It may not therefore be astonishing to learn that there exists a high frequency of primary liver cell cancer in Japan as well. But, in sharp contrast to the low incidence of gastric ulcer and cancer in the Malays, there is among the Japanese, particularly among males, an extremely high incidence of cancer of the stomach, so that cancer of the liver and of the stomach are together responsible for 75 per cent of the total cancer mortality in Japanese men. In Japanese women cancer of the stomach and liver are less frequent, but still represent 48 per cent of the total cancer mortality.

Cramer, in 1937, referring to these facts in his paper on "The Importance of Statistical Investigations in the Campaign Against Cancer," [1] pointed to another striking phenomenon in the statistics on cancer of Japan, namely, the exceptionally high incidence of cancer of the uterine cervix, which accounts for 32 per cent of cancer mortality among the women, coupled with the extremely low incidence of 3 per cent for mammary cancer. This, Cramer pointed out, is a condition not existing in any other country for which reliable statistics are available; one must agree with his statement that an investigation into the factors possibly responsible for the high incidence of cancer of the cervical portion of the uterus among Japanese women may yield information on the remote causes of cancer in that organ, which may be generally applicable and therefore of great importance.

C. General Incidence of Cancer.—Surprisingly, in view of all these racial differences in the incidence of cancer of various sites, international statistics do not reveal any racial differences in susceptibility to cancer in general. On the contrary, there is remarkable uniformity among the races with regard to the total incidence of cancer. Cramer stated that the differences in the frequency with which the various sites are attacked can be accounted for by the varying influence in different races of external conditions, habits and customs.

His view is supported by the findings of Snijders and Straub [51] and of Kouwenaar,[52] who studied the total cancer mortality among the Chinese and Javanese in a certain part of Sumatra. They came to the conclusion that, taking into account the different age distributions, no tangible difference could be observed in the total cancer death rate, as recorded in Western countries.

This interesting fact accords with Cramer's thesis that there seems to be a statistical law operating in such a way that "in a comparison of the cancer mortality of different populations an increase in the incidence in one particular organ due to a direct effect is associated with a diminished incidence in other sites of such an order that the total incidence for the two populations remains the same." [53] Cramer concluded that the coexistence of wide variations in organ incidence with approximately equal total incidence among various countries indicates that the different populations contain about an equal proportion of susceptible persons and that the organ incidence distributes itself over the susceptible moiety.

51. Snijders, E. P., and Straub, M.: Contributions to the Cancer Problem in the Tropics, Tr. Cong. Far East. A. Trop. Med. (1923) **5**:779-805, 1924.

52. Kouwenaar, W.: Comparative Cancer Statistics in Javanese and Chinese, Geneesk. tijdschr. v. Nederl.-Indië **72**:392-401, 1932.

53. Cramer, W.: Prevention of Cancer, Lancet **1**:1-5, 1934.

In other words, there appears to be a general susceptibility to cancer more or less evenly distributed among different populations, with an organ or site distribution determined most probably by an organ-specific or tissue-specific favorable "external" or "internal" cancerogenic environment. Once again the importance is stressed of research into the nature of the disposition to formation of tumors, not only as this may appear to be a general constitutional feature but (and perhaps even more significant) as the disposition is manifested by the formation of tumors in particular sites—that is, the localization factor.

Finally, I suggest that there seems to be possible another line of explanation than Cramer's for the phenomena under discussion: From a genetic point of view the observations just enumerated are highly interesting and call for research into the gene-frequency distribution, which is responsible for general susceptibility to cancer (apparently so stable) and for the factors governing localization of the disease (seemingly so unstable) in different populations.

Appropriate methods for such a study have been devised and are now well developed by the work of R. A. Fisher, J. B. S. Haldane, L. Hogben, L. H. Snyder and C. W. Cotterman in several areas of genetic research. So far as I am aware, no work of the kind has yet been undertaken in the field of cancer, but it is believed that such investigation may yield badly needed information on the general disposition to malignant growths as well as on the localization factors and on the role which heredity plays in both.

CONCLUSIONS AND SUMMARY

The complexity of factors noted in regard to the conditions just discussed prevails equally in most forms, types and sites of tumors. And, as the cases of cancer in which direct hereditary transmission can be traced are rare, admittedly they cannot provide a valid answer to the question of whether, or to what extent, inherited susceptibility plays a part in the general incidence of malignant growths. For disorders indicating a purely hereditary proneness to formation of tumor, such as xeroderma pigmentosum or neurofibromatosis, must be differentiated from many other types of tumor formation about which nothing yet is known of an inherited tendency, for example, cancer of the lip, which, according to Waaler, seems to be distributed independently of any inherited disposition.

Much remains to be done before these problems can be solved, but the task will be lighter if the lesson already taught is heeded, that it is vain to ask "Is cancer hereditary?" but that we must inquire separately for each organ, tissue and type of the disease whether any hereditary factors, direct or indirect, are involved in a specific form of the malady.

A summary of the present position meanwhile shows that enough evidence has been accumulated to warrant at least the following statements:

A. Cancer is not a unit disease, at least so far as its genetic behavior is concerned. Tumors of different sites and types differ in their genetic behavior.

B. Therefore it is unlikely that a heritable condition of "cancer" exists as such. Or, as Haldane [54] has put it: "The genetics of spontaneous cancer is clearly very complicated, and it is quite ludicrous to ascribe it to the activity of one gene, dominant or recessive."

C. There does exist a general inherited disposition, whether of susceptibility or refractoriness, to formation of tumor.

By the term "susceptibility" should be understood the ability of the body to react to specific stimuli with formation of tumor.

By the term "refractoriness" is meant a condition which seems to make the formation of tumors impossible even in the presence of appropriate stimuli.

D. In certain persons, factors exist, most probably inherited independently of a general disposition, which govern the localization of the disease. This localization in turn seems to depend on a favorable "internal environment" in certain tissues or organs.

E. If general susceptibility and inherited favorable internal environment are combined in an individual, these factors may be strong enough in themselves to lead to formation of cancer in certain tissues.

F. If general susceptibility is great in an individual, even relatively slight irritation by agents of many kinds may lead to formation of cancer.

G. But apart from these heritable conditions, there exist purely external cancerogenic agents of various kinds, which are obviously strong enough to lead to formation of cancer in certain tissues, even in persons in whom an inherited predisposition is not distinct or perhaps is too weak to be detected by methods used at present in testing for hereditary traits. Or the predisposition to cancer may not have been inherited but rather acquired under conditions the nature of which is not yet known.

54. Haldane, J. B. S.: The Genetics of Cancer, Nature, London **132**:265-267, 1933.

In this survey I have tried to give a picture of the situation of cancer research as seen from the viewpoint of a genetically minded physician. I am only too conscious that many important issues have not been touched on, for example, the mutation theory and the problem of polyploidy and their bearing on the question of development of tumor.

The chief aim of the survey has been to show that the whole problem of heredity and cancer is biologic and highly practical and not one to be dismissed after a somewhat barren discussion of comparative statistics and the mode of transmission. From the outline it will be clear that I am in agreement with MacDowell [55] (whose work on leukemia in the mouse is a fine example of the best genetic research), when he says:

> It is highly regrettable that, outside the immediate circle of geneticists, there seems to be an impression that the gene is self-sufficient and is either dominant or recessive. Especially as applied to neoplasia, this misunderstanding has led to erroneous conclusions both on the part of hostile critics and ardent believers. Dominance is only a special case at the end of a continuous series of interrelations between pairs of genes. No gene can produce its effect without cooperation of many other genes. . . . And, to repeat, genes and extrinsic conditions cooperate in all cases.

55. MacDowell, E. C.: Genetic Aspects of Mouse Leukemia, Am. J. Cancer **26**:85-101, 1936.

PILONIDAL CYSTS

CAPTAIN LAURENCE B. FELMUS, LIEUTENANT COLONEL CLIFFORD C. WOODS AND MAJOR DAVID H. SPRONG JR.
MEDICAL CORPS, ARMY OF THE UNITED STATES

The large increase in the number of pilonidal cysts coming to our attention for treatment, due to the concentration of military personnel, has stimulated a renewal of interest in this seemingly benign anomaly. Since the prime objective of a medical officer is to return every soldier to active service as soon as possible, the methods of treatment of this condition have entered the field of essential discussion and analysis.

Aside from the apparent increase in pilonidal infections resulting from military concentrations, there appears to be an actual increase in the number of infections in young men of the most vital military age group. Station and general hospitals frequently have special wards for these patients, and the length of hospitalization is an important factor, particularly in time of war. The physical strain and trauma resulting from necessary wartime training have caused many benign pilonidal sinuses to become infected and require treatment that otherwise might have remained dormant during the lifetime of a person leading a more sedentary existence. The men of military age are in the age group in which pilonidal infections are most common, and the direct trauma to the sacrococcygeal region to which men riding on the bouncing, hard seats of jeeps or trucks and paratroopers are subject is responsible for the onset of the infection.

All investigators agree that the anomaly is congenital, but its intriguing nature has resulted in numerous theories of its cause, many of which are fanciful.

In 1867 it was suggested by Warren that the condition was due to a changed polarity in the growth of hairs in the sacrococcygeal region and that the hairs grew inward underneath the skin, instead of growing outward. Later investigators, notably Tourneaux and Hermann [1] in 1887 and Mallory [2] in 1892, concluded that pilonidal sinuses resulted from coccygeal vestiges of the medullary tube. By means of serial sections through human embryos, Mallory was able to demonstrate histologically the neurogenic residua left after the spinal cord had been drawn cephalad relative to the downward thrust of the more rapidly developing vertebral column. This theory explained the undoubted presence of the coccygeal vestiges, first described by Tourneaux and Hermann, but did not explain the presence of hairs, which are found in about half of all pilonidal cysts and sinuses.

Oehlecker [3] in 1926 also demonstrated vestiges from the medullary canal which formed cysts and sinuses in the sacral region in the fetus but explained formation of pilonidal sinus with the presence of hairs as follows: The coccygeal tip of the curved embryo at the third month of embryonic development is firmly attached to the overlying skin (due to the lack of mesoblastic elements in this region at this stage) and is also connected to the underlying filum terminale of the periosteum of the medullary tube by means of the fibrous caudal ligament. The rapid downward thrust of the caudal tip causes a relative shortening of the caudal ligament and an invagination of the overlying skin, which is unable to keep up with the downgrowth of the coccyx. By the fourth or fifth month of fetal development, the skin which originally covered the tip of the coccyx is drawn upward so as to lie over the third or fourth caudal vertebra, and later it goes even higher. Almost all newborn infants exhibit a postnatal dimple in this region, but the production of a pilonidal sinus depends on the degree of invagination of the skin resulting from the traction, which is further increased by deposition of subcutaneous fat in the surrounding region and development of the nates. With complete invagination, the normal cutaneous appendages and products are also invaginated and rapidly accumulate to form cysts or are discharged intermittently as in fistulas.

However, clinically recognizable symptoms rarely occur before the age of sexual maturity, and this mode of development would result in a caudal direction of the sinus tract.

1. Tourneaux, F., and Hermann, G., cited by Mallory.[2]

2. Mallory, F. B.: Sacro-Coccygeal Dimples, Sinuses, and Cysts, Am. J. M. Sc. **103**:263, 1892.

3. Oehlecker, F.: Sacral Abscesses in Congenital Skin Displacements, Deutsche Ztschr. f. Chir. **197**:262, 1926.

A new slant on the formation of this congenital anomaly was provided by Stone in 1924 and expanded in 1931,[4] when he compared a sinus found in man with the preen gland which occurs in a great many species of birds. This was the first time that development of the sinus was stated to come from the outside as a normal cutaneous appendage from a downgrowth of special epithelium, unrelated to the vestiges of the medullary canal. Stone expressed the opinion that the coccygeal vestiges can never become so modified as to form skin, even though a cystic remnant should persist into adult life. The preen, or oil, gland serves as a special scent gland concerned with protection and sexual attraction of birds and consists of a number of straight tubules lined by polyhedral cells, which empty into a single small cavity communicating with the cutaneous surface through an epithelium-lined duct. In the mouth of the duct is found a small tuft of hairlike feathers, and the direction of the duct is cephalad, as in pilonidal sinus. Stone remarked that it may be assumed that in certain human beings latent potentiality for the formation of a glandular structure in the sacrococcygeal region analogous to birds, for some reason, develops into an actuality and results in the structure known clinically as pilonidal sinus. Further analogy is suggested by the time of development of pilonidal sinus, during early sexual maturity, both in birds and in human beings.

This line of reasoning was further confirmed in 1935 by Fox,[5] after extensive laboratory investigation with large numbers of pilonidal and embryologic specimens. His conclusions were:

> The pilonidal cyst is a congenital lesion due to a process of normal ectodermal invagination in the embryo, which usually disappears but in these cases has persisted in adult life. It commonly contains fine, silky, light colored hair, and mucoid or gelatinous material; is almost always infected, and its walls consist of several layers of epithelial cells with glands and hair follicles. Derived from budding or growth centers in the basal layer of the ectoderm which give rise to hair follicles and glands, it consists of cells which form only hair and glandular appendages. For this reason one never sees teratomata, neurogenic growths, or heterologous tumors in pilondial sinuses. The lesion becomes evident after the middle of the second decade and is probably associated with the development of secondary sex changes concomitant with puberty.

Gage,[6] in a well documented report, presented evidence to prove that pilonidal sinus results from an anomalous development of the medullary canal and that the coccygeal dimple results from disturbances in the development of the coccygeal ligament and is not connected with the medullary canal. Thus, he accepted the neurogenic theory of Tourneaux and Hermann and of Mallory for the cause of pilonidal sinus, and he accepted Oehlecker's explanation for the formation of the unrelated coccygeal dimple. Gage cited a series of cases and pathologic specimens illustrative of these conditions. The first case in his series, that of a child with a deep pilonidal dimple which disappeared after section of a fibrous tissue ligament beneath the skin, he cited to confirm Oehlecker's theory of the formation of the dimple by the pull of the caudal ligament. Successive cases were cited to illustrate increasing amounts of neuroglia tissue with increasing depth of the sinus extension. In 1 case, at reoperation, after a tract was carefully dissected into the sacral canal, the tissue was pulled on and severed with scissors; there was an immediate gush of cerebrospinal fluid into the wound. The entire wound was packed with iodoform gauze and loosely closed with sutures. Histologic examination revealed a sinus tract lined by stratified squamous epithelium, incompletely developed, but there were no cutaneous appendages, hair or sebaceous or sweat glands present. But he did find neuroglia. The patient recovered. The cases of Moise[7] and of Ripley and Thompson[8] were also described to illustrate failure of obliteration of the caudal end of the medullary canal, with persistence of a direct communication between the pilonidal sac and the cerebrospinal canal, complicated by staphylococcic meningitis. Moise proved his case by finding methylthionine chloride (methylene blue) which had been injected into the sinus in the cerebrospinal fluid. Continuous drainage was established by resecting the sinus and performing laminectomy. The patient recovered. In Ripley and Thompson's case pilonidal sinus occurred in a 3½ month old child and was verified at autopsy.

The importance of determining the cause of pilonidal sinus is evident, because the rate of recurrence of pilonidal infection following operative treatment is high and delayed healing is too frequent. Whether this recurrence of infection results from failure to dissect out all the finer

4. Stone, H. B.: The Origin of Pilonidal Sinus, Ann. Surg. **94**:317, 1931.

5. Fox, S. L.: The Origin of Pilonidal Sinus with an Analysis of Its Comparative Anatomy and Histogenesis, Surg., Gynec. & Obst. **60**:137, 1935.

6. Gage, M.: Pilonidal Sinus: An Explanation of Its Embryologic Development, Arch. Surg. **31**:175 (Aug.) 1935.

7. Moise, T. S.: Staphylococcus Meningitis Secondary to Congenital Sacral Sinus, Surg., Gynec. & Obst. **42**: 394, 1926.

8. Ripley, W., and Thompson, D. C.: Pilonidal Sinus as a Route of Infection in a Case of Staphylococcus Meningitis, Am. J. Dis. Child. **36**:785 (Oct.) 1928.

ramifications of the sinus, with subsequent regeneration, or from persistence of infection or bacterial contamination of the wound in an area which is difficult to keep bacteriologically clean, owing to the proximity of the anus, or from the poor blood supply in this region following formation of fibrous scar tissue or from a combination of these factors, we have succeeded in reducing the rate of recurrence far below that reported hitherto by careful attempts at elimination of all these possible causes.

The diagnosis of pilonidal sinus is made on the basis of the presence of one or more small openings in the midline or close to it over the sacrococcygeal region. Occasionally a tuft of fine, silky hair may be found protruding from the opening, and frequently when infection is present a foul-

A case of pilonidal sinus in which there were seven distinct fistulas.

smelling purulent material may be expressed. A probe may be inserted for varying distances, almost always cephalad, and frequently may go in the direction of a secondary sinus opening on the skin. In 3 of our patients secondary sinus openings were found on the left buttock. One patient presented seven individual and distinct fistulas, each one radiating to the sacrococcygeal region (figure). Each tract was dissected out and closed; healing was by primary union. Rarely, a cyst may be palpable in the sacrococcygeal region, and no pilonidal opening is visible, owing to early overgrowth of epithelium, which converts the pilonidal sinus from a fistula into a cyst. The patients are often hirsute and frequently unaware of the presence of the sinus, unless symptoms are caused by infection, usually following trauma of some kind.

The treatment of choice is surgical removal of the diseased tissue by wide excision, to include all ramifications of the burrowing tracts. Palliative treatment most often does not cure. In order to outline the finer ramifications, many operators have injected various dyes, india ink or paraffin, but Rogers and Hall[9] found this not only unsatisfactory and inaccurate but dangerous and unnecessary. The diseased tissue can usually be recognized by the naked eye, and often the dye stains blood vessels and normal tissue. In 3 instances a stained coccyx was removed, which on section failed to reveal any evidence of pathologic changes in the fascia of the bone. In other cases definite sinus tracts had been only partially filled and stained.

The chief divergence of opinion rests in the method of treatment of the resultant wound, following excision of the cyst. The wound may be left open to granulate and fill in with fibrous tissue; it may be closed primarily; or a combination of the two methods may be used.

Obviously, primary closure should not be employed in the presence of acute infection or when there is question of complete removal of all the diseased tissue. It may also be difficult or unwise to close primarily a wound too widely excised, if dead spaces cannot de obliterated.

At the Oliver General Hospital, except in cases of formation of abscesses, when incision and drainage are performed, frequently with cauterization of the walls of the cyst cavity, the procedure has been excision en bloc, with primary closure of the resulting wound.

Prior to the operation patients with either draining or nondraining sinuses are instructed to take sitz baths several times daily. The sacrococcygeal region is shaved, washed and painted with an antiseptic the day before operation and covered with a sterile towel. At operation, after careful preparation of the area, as little healthy tissue is removed as is consistent with complete excision of the sinuses and cyst. The general direction and depth of the tracts are determined by probing, at the onset. The open wound is then irrigated with saline solution of chloroazodin and frequently is dusted with buffered sulfanilamide powder. With careful attention to hemostasis and obliteration of dead spaces, closure is effected by means of nonabsorbable silk or cotton sutures of minimum tension. Undercutting of the skin has rarely been necessary, and the edges of the wound are usually

9. Rogers, H., and Hall, M. G.: Pilonidal Sinus. Surgical Treatment and Pathologic Structure, Arch. Surg. **31**:742 (Nov.) 1935.

approximated without too great difficulty when the adhesive tape straps, used to expose the pilonidal area and hold the nates apart, are released. A point is made of careful accurate apposition of the cutaneous edges. By means of a grooved director, inserted between two sutures at the lower angle of the wound, any retained blood is gently expressed, and the wound is then covered with either a strip of sulfanilamide film or bismuth tribromphenate gauze, over which is placed a gauze pressure dressing. Wide strips of adhesive tape are used to hold the dressing in place and prevent contamination from the anus. Patients are then instructed to be careful in defecation, that they do not carry infection upward.

Unless definite indications of infection arise, the dressing is unchanged for eight days, after which time a new dressing is applied after inspection and careful drying of the wound. Sutures are removed on the tenth day, and patients are permitted out of bed on the twelfth to the fourteenth day. After one week of ambulation in the ward, with a repetition of sitz baths, the patients are transferred to the reconditioning ward for an average of two weeks, prior to return to duty.

In case of reinfection, the wound is exposed earlier than in eight days, the sutures in the infected area are removed and the infection thereafter is treated daily with chloroazodin in oil packing and buffered sulfanilamide powder.

Generally, stress is placed on extreme cleanliness of the lower part of the back, with frequent shaving in this region and dressings to keep the skin between the nates dry.

In cases of recurrent sinus or persistent infection of an imperfectly healed wound, reoperation is performed exactly as outlined and as often as deemed necessary, after two or three week intervals and after the usual cleansing sitz baths.

COMMENT

Half of all the patients in our series fall into the age group of 21 to 25 years and one third into the age group of 26 to 30 years (table 1).

TABLE 1.—*Age Incidence*

18 to 20 years	14%
21 to 25 years	49%
26 to 30 years	29%
31 years or over	8%

Eleven per cent of the patients required repeated excision of the pilonidal area, when draining sinuses recurred. Twenty-four per cent of the patients in whom the wound failed to heal by primary union because of a breakdown in a portion of it were nevertheless discharged for duty in about fifty-one days following operation, having been cured by means of conservative treatment. We have found that healing is more rapid with primary than with secondary closure because of partial closure of the wound.

Table 2 summarizes the results of the first 100 patients treated at the Oliver General Hospital.

TABLE 2.—*Results of Excision*

Healed by primary union	65%
Healed by secondary union after primary closure	24%
Recurrences	11%
Average stay in the hospital, including 2 weeks of reconditioning	51.7 days

Occasionally patients have been returned from the reconditioning ward, where they had been transferred as cured, prior to return to duty, because of reinfection, which became apparent with marked increase in physical activity. This fact led us to speculate about the effects of full military activity on apparently healed sinuses. Reports [10] have appeared in the literature in which healing by primary union has been almost 100 per cent, without any follow-up information. Accordingly, a simple questionnaire was sent to the commanding officers of the patients returned to duty, requiring only a check to indicate whether the patient was performing full duty or whether it was necessary that he be rehospitalized (table 3). It was found that 57 patients were performing duty, 2 were rehospitalized and 6 were unidentified. Replies were not received concerning the remaining 35, many of whom, however, we have reason to believe are overseas performing full duty. Thus we may conservatively estimate, from the number of definite answers received, that recurrences developed in not more than 5 per cent of the patients discharged from the hospital.

TABLE 3.—*Replies to Questionnaire*

Returned to full duty	57%
Rehospitalized for recurrence of infection	2%
No replies received	35%
Lack of information about patient	6%

It is interesting to note that only 2 patients of the 54 who were admitted to the hospital without previous operation had recurrences; 1 of these was just being returned to duty at the time of writing after four operations, the last of which was performed by the open treatment method.

10. Camp, M. N., and Polites, N.: Symptomatic Pilonidal Cyst Operative Treatment, Am. J. Surg. **59**: 541, 1943.

Rogers and Hall,[9] in their series of 181 cases, reported that with primary closure the rate of recurrence in civilian patients who had never been operated on before was 31 per cent and in patients who had had a previous operation it was 100 per cent. Other writers have reported even larger percentages of recurrence with the primary suture method. An all-inclusive questionnaire of the members of the American Proctologic Society gave a rate of recurrence of 23.29 per cent with the primary suture method and a rate of only 1.13 per cent with the open method.

In our opinion the problem of pilonidal cysts and their delayed healing is one of infection rather than true recurrence of pilonidal sinuses. We have seen numerous instances of reinfection after reasonably certain surgical removal of all the pilonidal sinus and infected tissue. The "recurrent sinuses" differ from the true pilonidal sinus in that hairs are not found in the former, whereas one would reasonably expect to find hairs in about 40 per cent of the true recurrent sinuses. Primary closure shortens the stay in the hospital, often by many months, and in order to decrease chances for infection we have used various antiseptics before and after closure of the wound. The use of fine nonabsorbable sutures, with gentle approximation of the walls of the wound and cutaneous edges, has also aided in minimizing the chances for infection and in improving healing of the wound. We have used chloroazodin solution, buffered sulfanilamide powder and bismuth tribromphenate gauze to cover the incision. Despite these measures, reinfection has occurred. We are now planning to study a comparable series of cases in which penicillin will be used, both locally and generally, and in which the same careful surgical technic and postoperative care will remain unchanged.

SUMMARY

Follow-up inquiries about the first 100 patients with pilonidal cysts treated at the Oliver General Hospital indicate that about five per cent have been rehospitalized after discharge from the hospital.

The average stay in the hospital was fifty-one and seven tenths days following operation.

Good results are obtained by careful attention to surgical principles in the handling of tissues and to antibacteriologic details in postoperative care.

Successful treatment of pilonidal sinus, in our opinion, is primarily a problem of wound healing, regardless of the exact method of surgical removal. The ideal agent for combating bacterial contamination has not yet been found, nor are all the factors influencing the healing of granulating wounds fully understood.

RUPTURE OF INTESTINE CAUSED BY NONPENETRATING TRAUMA OF THE ABDOMINAL WALL

A REPORT OF CASES

GEORGE HALSEY HUNT, M.D.
Surgeon, United States Public Health Service
STATEN ISLAND, N. Y.
AND
JOHN N. BOWDEN, M.D.
Surgeon, United States Public Health Service
SAN FRANCISCO

It has been recognized for hundreds of years that nonpenetrating trauma of the abdominal wall may cause intestinal perforation. The trauma need not be particularly severe, and frequently it causes no gross lesion of the abdominal wall itself. In view of the tremendous number of adequate injuries sustained every day by any large group of workers, the conclusion is inescapable that a special combination of circumstances must be present to cause actual perforation. Presumably the loop of intestine must be filled with either fluid or gas and must be fixed against an unyielding portion of the posterior abdominal wall, so that it cannot slip out of the way of the traumatizing force; this in turn implies a force acting in just the right direction.

The importance of this uncommon lesion lies in the disparity between the apparent triviality of the blow and the serious consequences of a failure in diagnosis. One must always keep in mind the possibility that a seemingly minor abdominal blow may have caused actual perforation of the intestine. Such perforation may of course also result from more serious trauma, such as may be caused by an automobile accident, in which intestinal perforation is accompanied by other gross injuries; this paper, however, is principally concerned with the results of relatively minor trauma.

Early diagnosis is essential for proper treatment. In a group of 17 cases reported by Poer and Woliver [1] diagnosis and treatment were delayed more than twelve hours after the accident; in this group the mortality was 70 per cent. In 14 cases of their series, diagnosis was made early and prompt treatment was instituted, with a mortality of "only 35 per cent."

In cases of intestinal perforation accompanied by other severe injuries, the intra-abdominal lesion may easily be overlooked on preliminary examination; signs and symptoms of acute peritonitis, developing a few hours later, should immediately be recognized by the surgeon as a possible indication of intestinal perforation. With the type of injury considered in this paper, there is likely to be an interval of several hours during which abdominal symptoms are minimal and signs are confusing. The intestinal wall is sensitive only to distention, so that the perforation as such causes no symptoms; the symptoms are those of peritonitis, which will develop with greater or less speed, depending on a variety of factors, such as the site of perforation, the composition of the leaking intestinal contents and the amount of leakage.

Poer and Woliver [1] gave three mechanical explanations for the delayed appearance of symptoms:

1. Incomplete rupture: In many instances severe bruising of the intestinal wall occurs which sloughs through several hours or even days later because of the development of local necrosis. Spillage is facilitated by the onset of peristalsis after the intake of food or fluids.

2. The production of intestinal paresis by the injury, which inhibits peristalsis for a sufficient time to allow an exudate of plastic lymph to seal the opening. After the patient has recovered from primary shock or after the intake of food, peristaltic action is resumed, with consequent leakage. Cope [2] first described this interesting theory in 1914.

3. Prevention of leakage: Leakage may be prevented mechanically by the plugging of the opening by the mucosal layers or, in the case of complete transverse division, by contraction of the circular musculature of the divided ends.

Published with the permission of the Surgeon General, United States Public Health Service.

1. Poer, D. H., and Woliver, E.: Intestinal and Mesenteric Injury Due to Nonpenetrating Abdominal Trauma, J. A. M. A. **118**:11 (Jan. 3) 1942.

2. Cope, V. Z.: The Early Diagnosis and Treatment of Rupture of Intestine, Proc. Roy. Soc. Med. (Surg. Sect.) **7**:86, 1914.

Shock is generally not an outstanding feature in these cases. Some pain is usually present from the beginning; Counseller and McCormack [3] stated that the pain is usually constant, dull and aching, not colicky. They expressed the opinion that continued vomiting after recovery from shock is a valuable early symptom and rigidity is the most valuable single sign. Cope [2] stressed the importance of rectal tenderness, due to the gravitation of irritating intestinal contents into the pelvis. There is seldom enough free gas in the peritoneal cavity to obliterate hepatic dulness, but roentgen examination (made with the patient standing or lying on his side, with the x-ray beam directed horizontally) may be of value. Cope [2] stated that he would submit a patient to laparotomy if in the absence of thoracic and renal injury the following signs and symptoms were present: (1) severe abdominal pain persisting for six hours accompanied by vomiting, a gradually rising pulse rate, local rigidity and deep local tenderness or (2) absent or slight abdominal pain with a steadily rising pulse rate, especially if the patient is restless and listless.

In short, the two important points are: first, to keep in mind the possibility of intestinal perforation following even minor trauma to the abdominal wall and, second, to explore the abdomen promptly at the first sign of peritonitis. It is better to explore a few normal abdomens and maintain a mortality rate of 1 per cent or less than to miss one perforated intestine and deny the patient his only real chance of recovery.

The operative procedure is standard. Most of the perforations occur in the jejunum or ileum, and the incision should be planned to permit thorough exploration of the whole small intestine. Counseller and McCormack [3] advised examination of the bowel from one fixed point to another, a few inches at a time. If a perforation is found, it should be covered with a warm moist sponge and exploration continued. The reason for this is that multiple perforations may be present so close together that resection is advisable. If this should be the case, time would have been lost closing the first perforation.

The following cases were observed by us at the United States Marine Hospital, San Francisco, and are reported with the permission of Dr. S. L. Christian, medical officer in charge. The first 4 cases are instances of the uncomplicated type of injury, in which there was no trauma of the abdominal wall. The mortality rate, 25 per cent, in these 4 cases is comparable to the mortality rate of 35 per cent reported by Poer and Woliver.[1] The 1 patient with no injury of the abdominal wall who died was an elderly Negro with arteriosclerosis, whose usual blood pressure may have been higher than that recorded after his admission to the hospital. The coroner's autopsy failed to discover the reason for the suddenness of his death; he must presumably be considered the victim of surgical shock.

Cases 5 and 6 are illustrative of complicated intestinal rupture. In case 5 rupture of the jejunum by nonpenetrating trauma was accompanied by other severe injuries, which masked the abdominal symptoms and which made us believe that exploratory operation was contraindicated after abdominal symptoms did appear. The patient died in sudden shock thirty-five hours after admission to the hospital. In case 6 there was a wound of the abdominal wall with extrusion of viscera and intestinal rupture; the appearance of the intestine suggested a bursting type of rupture similar in mechanism to that in the other cases reported, rather than a direct laceration of the intestine by the traumatizing force.

The mortality rate is recapitulated as follows:

In 4 cases of uncomplicated rupture of the intestine by nonpenetrating abdominal trauma, the mortality rate was 25 per cent; in 1 case of rupture by nonpenetrating trauma complicated by other serious injuries, the mortality rate was 100 per cent; in all 5 cases of rupture by nonpenetrating trauma, the mortality rate was 40 per cent; in 1 case of rupture of the intestine accompanied or caused by penetrating trauma, the mortality rate was 0; the mortality rate in all 6 cases was 33.33 per cent.

REPORT OF CASES

CASES OF UNCOMPLICATED RUPTURE

CASE 1 (Hunt).—R. H., a white merchant seaman 56 years old, was admitted to the hospital at 10:40 p. m. on Nov. 28, 1940.

History.—The patient was injured about 3 p. m. on November 28 while at work on shipboard. He was struck in the right lower portion of the abdomen by the end of a wooden plank. The blow was apparently not severe; he had no pain at the site of injury but noticed a desire to urinate. After voiding clear yellow urine he experienced priapism lasting about one-half hour, accompanied by extreme tenderness of the testicles. He continued working until 4:30 p. m., then went home and had a drink of whisky and beer. He slept for about one hour and then awoke with severe sharp pains throughout the abdomen; in his words, he had a "hot, throbbing sensation in the stomach." He was nauseated but did not vomit. He was taken to the San Francisco Hospital by ambulance, given a hypodermic injection and then transferred by ambulance to the United States Marine Hospital. His family and personal history were noncontributory except for the fact that a left inguinal hernia had been present since 1933. This had always been reducible.

3. Counseller, V. S., and McCormack, C. J.: Subcutaneous Perforation of the Jejunum, Ann. Surg. **102**: 365 (Sept.) 1935.

Examination.—His temperature was 37 C. (98.6 F.), his pulse rate 90 and his blood pressure 140 systolic and 70 diastolic.

Abnormal Findings: The heart was somewhat enlarged, with a mitral systolic murmur. The abdomen was rigid, with generalized tenderness, which was direct and rebound and maximum in the lower portion of the abdomen. There was no ecchymosis or abrasion of the abdominal wall. A reducible indirect inguinal hernia was present on the left side. Small bilateral hydroceles were observed in the tunica vaginalis of the testis.

Course.—A tentative diagnosis of ruptured intestine was made, and immediate operation was decided on after consultation with Dr. Robert A. Jones, chief surgeon. The operation was started at 1:42 a. m., on November 29, with the patient under spinal anesthesia induced with 150 mg. of metycaine hydrochloride. The peritoneal cavity was opened through a lower midline incision. It contained at least a liter of greenish intestinal contents, resembling thin pea soup. On the antimesenteric border of the small intestine in the proximal third of the ileum there was a perforation about 8 or 9 mm. in diameter. The loop of intestine containing the perforation lay in the left lower quadrant of the abdomen. The terminal portion of the ileum seemed somewhat thickened and rather doughy, but there was no gross abnormality of the intestine in the region of the perforation. No enlarged mesenteric glands were seen, but careful search for them was not carried out. The spilled intestinal contents were sucked out as completely as possible. The perforation was closed transversely with a continuous through and through suture and interrupted Lembert sutures of fine chromic surgical gut. The peritoneum and the posterior sheath were closed with continuous no. 0 chromic surgical gut sutures. The anterior sheath was closed with interrupted "near and far" sutures of no. 0 chromic surgical gut. The skin was closed with interrupted vertical mattress sutures. One small Penrose drain was introduced beneath the anterior sheath and a second beneath the skin.

His condition remained good during and following the operation. Wangensteen suction through a Levine tube was instituted immediately after the operation and was continued until December 4, the fifth postoperative day. One cubic centimeter of a 1:4,000 solution of neostigmine methylsulfate was given every four hours for eight days; there was moderate distention for about one week. He had his first bowel movement, with the aid of an enema of saline solution, on December 2, the third postoperative day. Both drains were removed on the same day. His maximum temperature was 38.6 C. (101.5 F.), on the fifth and sixth days. He was discharged from the hospital on Jan. 4, 1941; at that time the wound was well healed, he was eating well and his bowels were moving well.

Case 2 (Hunt).—A. H., a Negro dock seaman 64 years old, was admitted to the hospital at 5:25 p. m. on Oct. 9, 1943.

History.—The patient was injured about 3 p. m. on October 9, when an empty garbage can toppled from a pile, striking him in the lower part of the abdomen. He had moderate abdominal pain; he stopped working and was sent to the hospital. On his arrival, he walked into the hospital, complaining only of slight pain in the lower part of the abdomen.

Examination.—His temperature was 37.2 C. (99 F.) taken orally, his pulse rate 70 and his blood pressure 220 systolic and 105 diastolic.

Abnormal Findings: The heart was enlarged to the left of the nipple in the fifth intercostal space. There was a snapping first heart sound, with a short systolic murmur and frequent extrasystoles. Some generalized abdominal tenderness was noted. There was no abrasion or ecchymosis of the abdominal wall.

Course.—On admission to the hospital the patient was examined by the officer of the day and thought to have merely a contusion. Three hours later, at 8:30 p. m., the abdomen was rigid, with acute direct and rebound tenderness across the lower part of the abdomen, and one of us was called. The diagnosis of ruptured intestine was made, and operation was begun at 10:15 p. m. with the patient under spinal anesthesia induced with 140 mg. of metycaine hydrochloride. A transverse incision was made just below the umbilicus, with division of the right rectus muscle. The peritoneal cavity contained several liters of fluid, some of which was clear and straw colored and some of which was bile-stained intestinal contents. There was a perforation 8 or 9 mm. in diameter on the antimesenteric border of the ileum about 50 cm. from the ileocecal junction. There was considerable edema, with punctate subserous ecchymosis of most of the mesentery of the small intestine. The appendix was bound down to the posterior surface of the cecum with old fibrous adhesions, and there was a definite kink in its middle third. There was considerable surface inflammation of the appendix. The peritoneal fluid was removed by suction, and the perforation was closed by suturing the intestine transversely with two rows of continuous sutures and one row of Lembert mattress sutures of no. 5-0 chromic surgical gut. The appendix was removed. The peritoneal cavity and the wound of the abdominal wall were frosted with 8 Gm. of sulfanilamide. The abdominal wall was closed in layers with no. 0 chromic surgical gut sutures plus through and through sutures of silkworm gut, without drainage. A smear of the peritoneal fluid showed staphylococci and streptococci. A culture showed an aerobic and facultative anaerobic hemolytic streptococcus. The patient went into rather severe shock as the perforation was being sutured but responded to ephedrine and left the operating room in fairly good condition. After his return to bed he again went into shock but improved after an infusion of plasma and 10 per cent dextrose solution. A Levine tube was passed into his stomach, and continuous Wangensteen suction was started. At 2 a. m. on October 10, his blood pressure was 210 systolic and 96 diastolic and his pulse rate was 64 and of good quality. At 5 a. m. he pulled out the Levine tube; this was reinserted. At 5:30 a. m. he was cold and clammy but sleeping quietly. His pulse rate was 78, his blood pressure 162 systolic and 84 diastolic and his respiratory rate 20. At 9:10 a. m. his temperature was 37.2 C. (99 F.) taken orally, his pulse rate 92, his respiratory rate 20 and his blood pressure 110 systolic and 84 diastolic. He was restless, cold and clammy. He was given 250 cc. of plasma and 1,000 cc. of 10 per cent dextrose solution intravenously and 4 cat units of digalen intramuscularly, with some improvement. At 3 p. m. his blood pressure was 110 systolic and 80 diastolic. He died suddenly at 4:55 p. m.

Autopsy.—Postmortem examination was performed by the coroner. There was hypertrophy of the left ventricle of the heart, with marked dilatation of the right side of the heart. There was diffuse sclerosis of the aorta. The coronary vessels were small and sclerotic, and in the left circumflex coronary artery about 1 cm. past the bifurcation there was a heavy sclerotic plaque, opposite which there was a small postmortem thrombus. The abdominal viscera was covered by a fibrinopurulent exudate. No unsutured perforations were found.

CASE 3 (Hunt).—H. S., a white Coast Guard seaman 32 years old, was admitted to the hospital about 6:30 p. m. on Oct. 10, 1943.

History.—About three hours before admission he was running to catch a football, while looking back over his shoulder, when he ran into the tailgate of a truck, striking the upper part of the abdomen heavily. He had severe abdominal pain, which could be partially relieved by bending double. He was brought by ambulance several miles to the hospital. There were some nausea and vomiting. At the time of admission he complained of severe midabdominal cramping pain.

Examination.—His temperature was 37 C. (98.6 F.) taken orally, his pulse rate 90 and his blood pressure 130 systolic and 85 diastolic.

Abnormal Findings: Boardlike abdominal rigidity with direct and rebound tenderness, which was maximum in the umbilical region, was noted. There was no abrasion or ecchymosis of the abdominal wall.

Course.—The diagnosis of ruptured intestine was made, and immediate operation was done, with the patient under spinal anesthesia induced with metycaine hydrochloride. A transverse incision was made just below the umbilicus, with division of the left rectus muscle. The peritoneal cavity contained a small amount of brownish fluid as well as bile-stained intestinal contents. The small intestine, the transverse and the descending colon and the bladder were inspected. The only lesion was a perforation 1.5 to 2 cm. in diameter on the antimesenteric border of the jejunum about 15 cm. distal to the ligament of Treitz. The edges of the perforation were everted, and there was a tear of the serosa extending distally from the perforation for about 1 cm. The appendix was bound down to the posterior surface of the cecum with old fibrous adhesions. There was a kink in its middle third and some surface inflammation. The peritoneal fluid was removed by suction, and the perforation was repaired by suturing the wall transversely with two rows of continuous sutures and a third row of interrupted Lembert mattress sutures of no. 5-0 chromic surgical gut. The appendix was removed. The peritoneal cavity and the wound of the abdominal wall were frosted with 4 Gm. of sulfanilamide. The peritoneum and the posterior sheath were closed with contiuous no. 0 chromic surgical gut sutures and the anterior sheath and the aponeuroses with interrupted sutures of the same material. The skin was closed with silkworm gut sutures, four of which included a figure-of-eight bite of the anterior sheath. The spinal anesthesia at no time gave complete relaxation and wore off as closure was started. Supplemental anesthesia induced with pentothal sodium and with ether (given by the open drop method) was instituted, but before relaxation could be obtained there was considerable straining, with protrusion of viscera through the wound. These were protected with warm moist sponges, but this incident may have contributed to the later development of a pelvic abscess. A smear and a culture of the peritoneal fluid showed no organism. A Levine tube was passed into the stomach, and continuous Wangensteen suction was begun. He was given parenteral fluids, and 1 cc. of a 1:4,000 solution of neostigmine methylsulfate was given intramuscularly four times a day for five days and then twice a day for several more days. No distention developed at any time. He had a good bowel movement with the aid of an enema of saline solution on the fourth postoperative day, and the Wangensteen suction was discontinued on the fifth day. Sutures were removed on the tenth day. At this time a stitch-hole abscess near the left angle of the wound was found and evacuated. Moderate drainage persisted for about six weeks. On the twelfth day mild diarrhea developed, and he complained of suprapubic cramping pain. On rectal examination a tender bulging mass anterior to the rectum just above the prostate was found. He was given sulfathiazole by mouth (1 Gm. every four hours) from the twelfth to the twenty-fourth day. The pelvic abscess gradually became smaller and finally disappeared. He was discharged from the hospital on December 14, and it was considered that he would be fit for regular duty on Jan. 1, 1944. At the time of discharge the abdominal wound was completely healed, and rectal examination showed no abnormality. His appetite was good, and his bowels were moving normally.

CASE 4 (Bowden).—L. F., a white coastguardsman 18 years of age, was admitted to the hospital on April 9, 1944 at 8:50 p. m.

History.—The patient was injured at 6 p. m. on April 9 while riding in a midget speed car at an amusement park. The midget car jumped the track and hit a light post. The car was traveling at a speed of about 10 to 15 miles per hour. In the impact, his abdomen struck the steering post of the car. He had immediate agonizing pain in his abdomen. After a few minutes, however, he got up and walked out of the park onto the street, where he collapsed a few minutes later. He was taken to the emergency hospital and then brought to the United States Marine Hospital, arriving at 8:50 p. m.

Examination.—His temperature was 37 C. (98.6 F.), his pulse rate 72 and his blood pressure 120 systolic and 80 diastolic. He was examined by the officer of the day, who found tenderness in the left upper quadrant of the abdomen but no rigidity or rebound tenderness. It was the opinion of the doctor at this time that there was no evidence of intra-abdominal injuries.

Course.—When the patient was seen at 8 a. m. on April 10 by the ward surgeon, his temperature was 37.8 C. (100.04 F.) and his pulse rate 120. There were definite tenderness and rigidity in the upper portion of the abdomen, which were more pronounced on the right side. Diagnosis of peritonitis due to intra-abdominal hemorrhage or rupture of a hollow viscus was made. At 10 a. m., with the patient under spinal anesthesia induced with 120 mg. of metycaine hydrochloride which was supplemented by cyclopropane, an upper right rectus incision was made. When the peritoneum was opened a small amount of free fluid was encountered, and there was evidence of a mild general peritoneal reaction. The retroperitoneal space at the level of the duodenum was distended, and there was severe inflammatory reaction of the tissues about the duodenum and head of the pancreas, with some fatty necrosis of these tissues. The stomach and the first portion of the duodenum were normal. The peritoneum at the right lateral edge of the upper portion of the second duodenal segment was divided (Kocher's maneuver), and the descending duodenum was exposed by turning it forward, downward and to the left. This brought the posterior surface of the descending duodenum into view. There was a perforation approximately 5 mm. in diameter at this point. This perforation was closed with interrupted sutures of no. 5-0 chromic surgical gut, the stitches being placed transversely. Two reenforcing sutures of silk were used also. The pancreas was examined, and no evidence of injury to this organ was found. The rest of the intestinal tract was examined, and no abnormality was discovered other than severe distention of the entire large intestine. A Penrose drain was placed posterior to the duodenum and brought out through a stab wound in the right flank. A few interrupted no. 0 chromic surgical gut sutures

were placed in the peritoneum at the lateral edge of the duodenum. The wound was closed with through and through silkworm gut sutures and the peritoneum with a running suture of no. 0 chromic surgical gut. Continuous Wagensteen suction was begun, and treatment with penicillin, 10,000 units every four hours, was started. The postoperative course was good, and on the sixth postoperative day the highest temperature was 38 C. (100.4 F.) and the pulse rate 90. On this day Wangensteen suction and administration of penicillin were discontinued. He was then allowed to have liquids by mouth, and on the eighth postoperative day he was given a soft diet. The drain had been removed on the fourth postoperative day. The tract continued to drain for approximately two weeks. Cultures taken from the material drained from the tract gave negative results. At the end of two weeks the drainage tract and the abdominal wound had completely healed. His postoperative course was smooth until May 1, when he began to have fever. At the same time he complained of some tenderness over the left femoral vein, and evidence of mild phlebitis was found. The fever gradually subsided, and on May 21 the patient had no complaints and his temperature and pulse were normal. He was taking a liquid diet without difficulty and was up and about the ward.

CASES OF RUPTURE COMPLICATED BY OTHER INJURIES

CASE 5 (Bowden).—T. M. McG., a white carpenter 46 years old, was admitted to the hospital at 11 a. m. on Nov. 9, 1943.

History.—The patient was injured at 10:30 a. m. on November 9 while at work in a ditch about 5 feet (1.5 M.) deep. The sides of the ditch caved in, burying the patient up to his shoulders in large stones and clay. The handle of his shovel was forced against his abdomen by the weight of the surrounding earth. The patient was dug out of the ditch and brought to the hospital immediately. He stated that en route to the hospital he noticed that he was unable to move either leg. Most of the pain at the time of admission to the hospital was located in the lower portion of the abdomen, and there was general abdominal discomfort. His family and personal history were noncontributory.

Examination.—His temperature was 36.8 C. (98.2 F.), his pulse rate 100 and his blood pressure 130 systolic and 85 diastolic.

Abnormal Findings: There was complete paralysis of the lower extremities, with anesthesia below the level of the iliac crest on both sides. There was moderate abdominal tenderness but no distention or rigidity. There were definite tenderness in the pelvic region and swelling in the right inguinal region. There were an abrasion on the back in the upper lumbar region and some pain on compression of the thoracic cage.

Course.—A roentgenogram, taken soon after the patient's admission to the hospital, revealed comminuted fractures of both rami of the pubis on the left side and complete separation of the left sacroiliac joint. There were a fracture through the body of the pubis on the right side, a fracture through the lateral mass of the sacrum and also a fracture involving the posterior inferior and superior spines of the ilium. Soon after hospitalization the patient was catheterized. His urine was clear. In view of paralysis and sensory changes in the lower extremities, the possibility of concussion of the spinal cord was considered. However, in about four hours the patient was able to move his feet and legs, and the anesthesia disappeared from the right lower extremity, but there was still complete anesthesia of the left lower extremity. During most of this time there was no definite symptom referable to the abdomen. His white blood cell count was 6,000, with 79 per cent neutrophils. The next morning the paralysis of his lower extremities was still less extensive, but hypesthesia persisted over the lower extremities. He was seen at this time by the neurosurgical consultant, who was unable to account for the findings other than to suggest the possibility of vascular embarrassment, secondary to compression of the trunk and abdomen, and advised conservative treatment and further observation. During the morning of the second day, he began to complain of abdominal pain, and examination revealed tenderness over the right side of the abdomen and some rigidity. His condition at that time was not good. His blood pressure was 130 systolic and 90 diastolic, his temperature 36 C. (96.8 F.) and his pulse rate 120. We considered the possibility of general peritonitis, probably on the basis of hemorrhage into the peritoneum. (Because of the severity of the bony injuries and the persistence of hypesthesia and partial paralysis of the lower extremities, exploration of the abdomen was not considered advisable.) At 10 p. m. on November 10 the patient suddenly went into deep shock and despite efforts to revive him died at 10:25 p. m. Autopsy was performed by the coroner, who reported fractures of the pubic bone, separation of the left sacroiliac joint and rupture of the jejunum with peritonitis.

CASE 6 (Bowden).—D. W., a 47 year old Negro male laborer, was admitted to the hospital at 4 p. m. on April 11, 1944.

History.—At 2:30 p. m. on April 11 the patient was driving a tractor down a steep ramp, when he lost control of the machine. The tractor ran over the edge of the ramp and turned over against a concrete wall, catching the patient in the abdomen between the machine and the wall. There was a knob on the steering wheel of the tractor, and the patient thought that this knob caught him in the right lower portion of the abdomen.

Examination.—His temperature was 37.2 C. (99 F.), his pulse rate 100 and his blood pressure 138 systolic and 70 diastolic.

Abnormal Findings: The patient's general condition was good. There was an incision in the right lower part of the abdomen, beginning just above the anterior superior spine and running transversely toward the midline. There were several loops of large and small bowel lying on top of the abdomen, and these were covered with spilled intestinal contents.

Course.—The patient was taken to the operating room immediately, and, with him under spinal anesthesia induced with 100 mg. of metycaine hydrochloride, the loops of intestine lying on top of the abdominal wall were examined; a perforation approximately 5 mm. in diameter on the antimesenteric border of the ileum about 2 inches (5 cm.) from the ileocecal valve was found. There was little or no evidence of trauma to the intestine surrounding this perforation, and it was our impression that the bowel had been ruptured from the pressure within its lumen, rather than from external trauma. The exposed intestines were then thoroughly irrigated with a large amount of isotonic solution of sodium chloride. The surrounding skin was prepared, and the perforation in the ileum was then repaired with a Connell suture of no. 5-0 chromic surgical gut for the first layer and an interrupted Lembert type of suture for the second layer. The sutures were placed transversely. After the rest of the bowel had been examined, it was returned to the peritoneal cavity. The wound was enlarged to facilitate exploration of the peritoneal cavity. A tear in the posterior part of the peritoneum over the psoas muscle

exposed this muscle and the right ureter. The tear in the peritoneum was repaired with a running suture of no. 5-0 chromic surgical gut. No further injury or evidence of disease in the intestines or intra-abdominal organs could be found. The wound was then closed in layers, a running suture of no. 0 chromic surgical gut being used for the peritoneum and interrupted mattress sutures being placed through the muscle to close the muscle and fascia. A Penrose drain was inserted into the wound.

The patient was returned to the ward in good condition, and continuous Wangensteen suction was begun. He was given 5 Gm. of sodium sulfadiazine intravenously, and intravenous administration of sodium sulfadiazine every eight hours was started. For the first five days his temperature was elevated, but never to a point higher than 38.5 C. (101.3 F.), and the highest pulse rate recorded was 120. There was no abdominal distention, and by the sixth postoperative day the patient's condition was satisfactory. The Wangensteen suction was discontinued, and on the eighth day sodium sulfadiazine therapy was stopped and administration of 1 Gm. of sulfadiazine every four hours by mouth was begun. The drain was removed from the wound on the third postoperative day, and by the seventh postoperative day there was evidence of infection in the wound. However, it was adequately drained and subsequently showed continuous improvement. The patient's temperature was normal after the twelfth postoperative day, and except for the fact that the wound was not perfectly healed his condition on May 24 was normal.

EPITHELIZATION OF EXPERIMENTAL WOUNDS

FRANK L. APPERLY, M.D., D.Sc., AND M. KATHARINE CARY, A.B.
RICHMOND, VA.

The healing of wounds is a complex phenomenon, involving such apparently diverse processes as proliferation of new capillaries, fibroblasts and epithelial cells. In addition, production of antibodies and phagocytosis may be involved. Much experimental work has been done to elucidate the conditions governing these processes. We are here concerned only with certain aspects of epithelization.

In an attempt to obtain a clue which might lead us to the discovery of those factors which promote the healing process, we considered the various processes and therapeutic procedures which by long experience are known to be most effective in the treatment of infections and wounds, with the object of discovering some factor or factors common to all. On the whole it seemed to us that these processes had in common the effect of rendering or tending to render the blood and tissues of the patient more alkaline. Conversely, those conditions which appeared to be associated with increased vulnerability to injurious influences seemed to be acidifying.

The table classifies all of those conditions which are associated with, or which lead to, an alteration of plasma p_H and carbon dioxide content. Those conditions associated with increased resistance and efficiency of healing fall, in general, into types *d* and *b*, in both of which the blood plasma is more alkaline. Similarly those conditions associated with diminished resistance and poor or delayed healing fall generally into type *c*, in which the blood plasma is more acid.

Published experimental clinical reports are equivocal. Favoring the thesis that increased alkalinity promotes healing are the reports that fibroblasts grow best at a p_H of 7.4 to 7.8,[1] that increased p_H favors healing [2] and increases resistance to tuberculous infection,[3] that external application of dilute solution of ammonium bicarbonate favors healing of wounds [4] and that healthy granulation tissue is alkaline, even up to p_H 8.3.[5]

On the other hand, others have reported that healing wounds are acid,[6] that acidity promotes healing by limiting bacterial infection [6] and that

Classification of Conditions Known to Be Associated with Alterations in Blood p_H and Carbon Dioxide Content

(a) Increase of plasma CO_2 content with diminished p_H Breathing of CO_2 Emphysema of lungs Some chronic cardiac diseases	(c) Diminution of plasma CO_2 content with diminished p_H Following ingestion of acids (NH_4Cl, etc.) Chronic nephritis Diabetes Pregnancy Menstruation Starvation Severe exercise with exhaustion Severe anemias and leukemia Debility Hepatic cirrhosis Some chronic cardiac diseases, especially congenital morbus cordis
(b) Increase of plasma CO_2 content with increased p_H Following ingestion of alkaline salts (sodium bicarbonate, citrate, etc.) and insulin	(d) Diminution of plasma CO_2 content with increased p_H Hyperpnea with hyperventilation Warm climates High altitudes Artificial fever Local heat with hyperemia General roentgen irradiation Allergy (?)

From the Department of Pathology, Medical College of Virginia.

1. Fischer, A.: J. Exper. Med. **34**:447, 1921.
2. Holmes, A. D.: New England J. Med. **227**:909, 1942.
3. Petersen, W. F.; Howe, J. S., and Milliken, M. E.: Am. Rev. Tuberc. **44**:377, 1941.
4. Robinson, W.: Am. J. Surg. **47**:111, 1940.
5. Schade, H., and Claussen, F.: München. med. Wchnschr. **73**:343, 1926.
6. Waugh, W. G.: Brit. M. J. **2**:236, 1941.

this state can be maintained by acid-forming diets [7] and by administration of ammonium chloride.[8]

In reinvestigating this problem we decided (1) to limit our observations to the rate of epithelization and (2) to attempt to influence the tissues via the blood, by using such simple substances as ammonium chloride and sodium acetate,

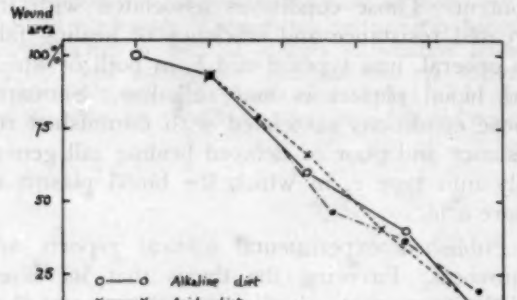

Fig. 1.—Chart showing the average rates of epithelial coverage of experimental wounds in three groups of rats fed acid and alkaline diets.

which are known to produce acidemia and alkalemia if given in sufficient doses, but in our experiments to limit the doses of these salts to "practical" amounts, i. e., by adding them to the drinking water of our animals in sufficient quantity to make a solution of 2 per cent. Greater concentrations than this could not be used satisfactorily in ordinary practice, on account of nausea and vomiting.

METHODS

The standard wound was made by the application of a circular loop electrocautery to a shaved and sterilized area below the scapular area of a rat, i. e. in a position where it could not be interfered with by the animal. The circular patch of skin and fascia, 13 mm. in diameter, was removed with scissors from the underlying muscle and trimmed clean, and the edge of the wound was fixed to the muscle by lightly touching it with a small knob cautery. No dressing was used for the wound. Seventy-two hours later measurements were made by tracing the outline on a glass slide with a fine pen, projecting through a photographic enlarger which gave a magnification of × 10; the area was measured with a planimeter. The first area measured was called 100 per cent. Measurements were repeated every few days until healing was nearly complete.

Three groups of animals were used, all of which were fed the usual laboratory standard diet, but with an acidifying or alkalinizing solution (2 per cent) substituted for drinking water. This diet was commenced seven days before the wounds were made. Three groups of rats were observed: (*a*) Thirteen rats received ammonium chloride solution; (*b*) 12 rats received sodium acetate solution, and (*c*) a control group received water.

Figure 1 shows the results. The three curves represent the average rate of epithelization in each of the three groups and provide data for studying: (*a*) the effects, if any, of acidification and alkalinization on the rate of epithelial growth; (*b*) some aspects of the mechanism of epithelization.

THE EFFECT OF ACIDIFYING AND ALKALINIZING SALTS, ADMINISTERED BY MOUTH, ON EPITHELIZATION

The three curves almost coincide; they show that the rate of epithelization is unaffected by acid and alkaline salts taken by mouth in the doses used by us. Since the salt solutions provided the only fluid imbibed by these animals for twenty-five days, it would appear that, whatever effects these salts might produce under extreme experimental conditions, their effects were practically nil under the conditions of our experiments.

SOME ASPECTS OF EPITHELIZATION

Since all three curves practically coincide, we can assume that they represent fairly closely the

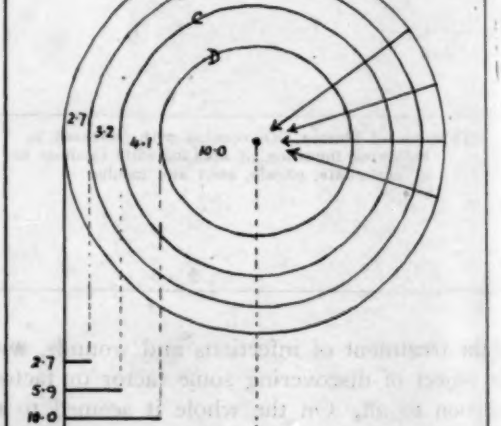

Fig. 2.—Chart showing increasing daily centripetal growth of epithelium, but with constant coverage, in experimental wounds.

rate of epithelization in rats under normal conditions. The fact that the average curve is a straight line, except during the first three or four days and at its termination, shows that the same percentage of the original area is covered per day, in spite of the fact that the length of the edge of new epithelium becomes progressively

7. Herrmannsdorfer, A.: Deutsche Ztschr. f. Chir. **200**:534, 1927.

8. Reimers, C., and Winkler, H.: Deutsche Ztschr. f. Chir. **241**:313, 1933.

shorter. Figure 2 diagrammatically represents the growth on three successive days. Each ring represents the epithelial edge at the beginning of each day. The areas between the rings are equal; i. e., they represent the total coverage each day. It is obvious, however, that the distance covered radially toward the center increases each day in inverse proportion to the length of the edge of new epithelium. What does this mean? Are the cells on the continuously diminishing edge proliferating proportionately faster in order to cover the same area, (proliferative activity increasing with time)? Or are the epithelial cells being pushed or migrating centerward? The latter supposition would imply that the proliferating cells are on the original periphery and do not change place, i. e., that the process resembles that in normal skin, in which the proliferating basal cells push the older cells toward the outer surface, whereas in wounds the old basal cells push the epithelium as a sliding sheet across the wound toward the center. The latter explanation is supported by the observations of Loeb,[9] who found the mitotic activity confined to the "back areas" (the original periphery), at some distance from the advancing epithelial edge.

Since our work has been completed, Henshaw and Meyer[10] have published their results, with an excellent summary of earlier work, which we have therefore omitted from this paper. We agree with them that the rate of proliferation of the basal cells is constant during most of the period of healing (represented by the straight part of the curves in figure 1) and that therefore the time of coverage of a long narrow wound would be determined by their formula $T = \frac{L}{V}$, in which T is the total healing time, L the initial breadth of the wound and V the rate of advance of the epithelial edge per day.

When, however, the wound is circular, or the periphery is short compared with the area, and the peripheral basal cells are pushing the epithelium toward the center (fig. 2) the increasing lateral pressure of the converging "columns" of cells would be expected to accelerate the forward movement of the "head" of each converging "column," i.e., V, or the distance traveled each day toward the center, to increase with time. Our experiments show this to be true. Their formula therefore does not hold true for this type of wound.

Henshaw and Meyer[10] further stated that the healing of irregular wounds is a function of neither the length of the growing edge nor the area of the wound but of the diameter of the largest circle that can be described within the edges of the wound. The matter is not as simple as this. Since growth of the basal cells pushes out the epithelial sheets in a direction at right angles to the growing edge (shown by arrows at *A* and *B* in figure 3), it follows that at *A*, where the lines of growth converge, the distance traveled toward the center, *C*, will be considerably greater than the distance traveled from segment *B*, where the lines of growth diverge. It would seem that no simple formula will describe the time of wound healing unless the wound is of such a simple shape that the area can be readily calculated.

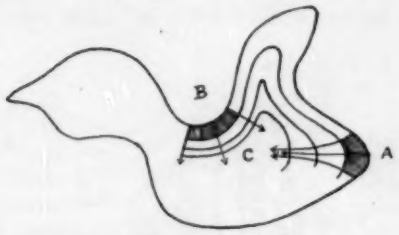

Fig. 3.—Drawing showing variations of centripetal growth of epithelium on convex and on concave segments of the periphery of a wound.

REGULATION OF GROWTH

Although we have no intention of discussing the various theories of growth and the factors regulating it—of which the best known are those of Carrell[11] and of Burrows[12]—certain interesting considerations arise from the foregoing observations.

One of these is the reason for the slowing down and final cessation of the growth of basal epithelial cells, represented by the flattening out of the terminal part of the growth curve (omitted from figure 1). As the growing cells push the enlarging epithelial sheet across the wound, especially when the lines of growth converge with an increasing lateral squeeze, resistance to, or pressure on, the proliferating cells must also increase. Since pressure on growing tissues elsewhere leads to diminution and cessation of

9. Loeb, L.: Arch. f. Entwcklngsmechn. d. Org. **6**:297, 1898.

10. Henshaw, P. S., and Meyer, H. L.: J. Nat. Cancer Inst. **4**:351, 1944.

11. Carrel, A.: J. Exper. Med. **15**:516, 1912; Proc. Inst. Med. Chicago **8**:62, 1930.

12. Burrows, M. T.: J. M. Research **44**:615, 1924; Am. J. Anat. **37**:289, 1926.

growth and even atrophy and, conversely, since the release of lateral intercellular pressure (as in wounds) leads to further growth, one would expect mutual cellular pressure to be a factor in some way regulating growth, probably by mechanically interfering with the inflow or supply of nutrient and growth-stimulating substances (creatine, sulfhydryl compounds, etc.) and with the outflow of waste products, which, as is known from observations on tissue cultures, diminish cellular growth. If these things are true, then healing wounds are self regulating.

CONCLUSIONS

From these considerations we conclude that: (*a*) with a constant rate of epithelial proliferation, the area covered per day depends only on the length of the periphery of the wound; (*b*) for wounds with a high ratio of periphery to area (long, narrow wounds) a simple formula based on the breadth of the wound can be used for calculating healing time, and (*c*) for wounds with a low ratio of periphery to area (broad wounds) a formula based on the more complicated measurement of area must be employed.

DIFFERENCES IN THE PATTERNS OF BITES OF VENOMOUS AND OF HARMLESS SNAKES

CLIFFORD H. POPE, B.S., AND R. MARLIN PERKINS
CHICAGO

Some students maintain that when a pit viper bites in self defense it merely sticks its fangs into the victim as a stab, whereas others insist that such a snake uses both its jaws in a true bite. Early reports of the last century, such as the classic ones of Weir Mitchell and Joseph Fayrer, vaguely describe pit vipers as actually biting, but the fact was not emphasized because then much more important aspects were crying for attention. Nearly all recent instructions for the treatment of snake poisoning flatly state that the bite of a venomous snake leaves only one or two fang punctures and is therefore readily distinguished from that of a harmless one, with its six rows of punctures made by small teeth (fig. 1). The purpose of this paper is to settle the question, which has practical value in the treatment of snake poisoning as well as theoretic interest.

If a venomous snake leaves but two marks, there can be no doubt about its identity and just where the first aid cuts should be made; if many marks are left by either a poisonous or a harmless snake, the victim, already suffering from tremendous nervous strain, may be called on to exert considerable judgment in determining the nature of the bite and then, in case it is dangerous, finding the fang punctures.

In the United States, all poisonous snakes except two kinds of coral snakes are pit vipers. Since coral snakes never strike but inject their venom by seizing a victim at close range and chewing, they have been left out of consideration; obviously the pattern of their bite is a separate problem. The pit viper of the United States that inflicts the greatest number of serious bites is the western diamond-back rattlesnake (Crotalus atrox); hence this species was chiefly

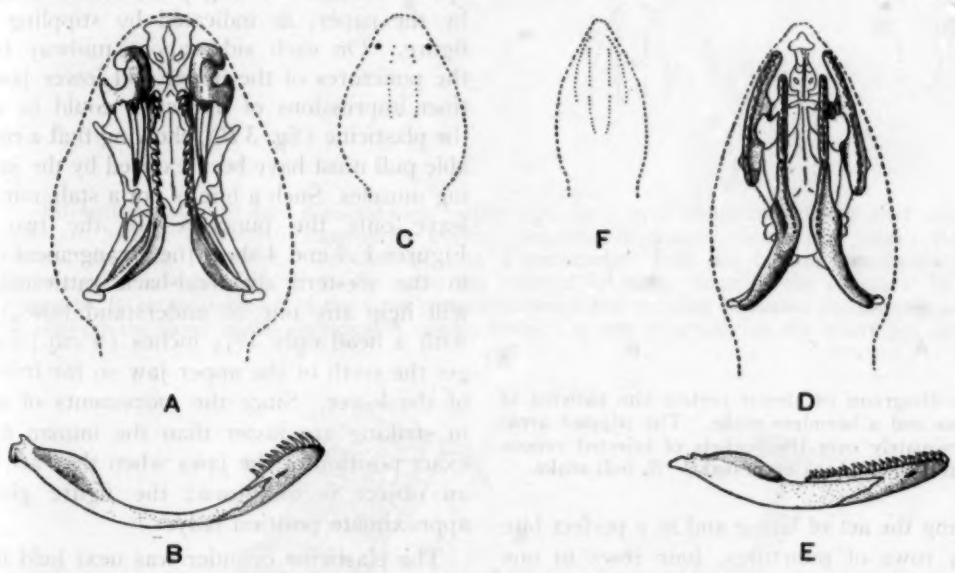

Fig. 1.—Teeth of a harmless snake compared with teeth and fangs of a venomous one. *A*, upper jaw of a western diamond-back rattlesnake seen from below, showing the fangs folded and the two rows of teeth lying between the fangs, each row being made up of three teeth on the palatine bone and eight on the pterygoid bone. *B*, side view of one arm of the lower jaw, with its ten teeth. *C*, diagram of the arrangement of the teeth and fangs in the same upper jaw, each fang being represented by a heavy black spot. *D*, teeth in the upper jaw of the bull snake, a harmless domestic species. The two inner rows are longer than in the rattler, since the bull snake has seven more teeth on the palatine and two more on the pterygoid bone. The bone that in the rattler serves as a base for the fangs carries sixteen teeth in the bull snake. *E*, one arm of the lower jaw, which has twice as many teeth as that of the rattlesnake. *F*, diagram of the arrangement of the teeth in the bull snake.

used in the demonstrations. Conclusions based on it are no doubt valid for other rattlesnakes in the United States. The pit vipers of the United States lacking the rattle are the water moccasin (Agkistrodon piscivorus) and the copperhead (Agkistrodon mokasen), and a representative of each of these was also used to complete the list of domestic pit vipers. Since Klauber has suggested that some tropical American kinds bite in a somewhat different manner, it may be best to refrain from generalizing about pit vipers other than those of the United States.

All of the harmless snakes in the United States big enough to bite have four rows of teeth in the upper jaw and two in the lower. Figure 1 *D*, *E* and *F* shows the arrangement of the teeth in the bull snake (Pituophis sayi), a harmless species. Since the teeth in any one of the harmless snakes are usually similar in size, structure and shape, most of them come into play during the act of biting and in a perfect bite leave six rows of punctures, four rows in one group and two in the other (fig. 2 *B*). In the pit vipers, the outer row on each side of the upper jaw has been reduced to a single large, erectile, hollow tooth, the fang. The bite of a pit viper, therefore, should leave not more than four rows of punctures in addition to the two large perforations made by the fangs (fig. 2 *A*).

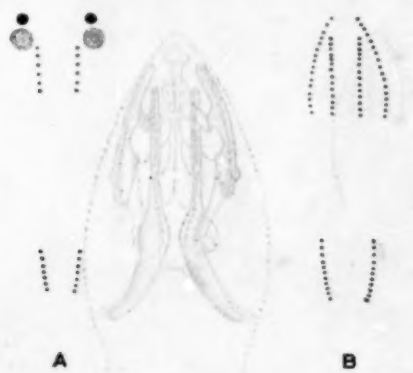

Fig. 2.—Diagrams of almost perfect bite patterns of a poisonous and a harmless snake. The stippled areas are approximately over the pockets of injected venom. *A*, western diamond-back rattlesnake. *B*, bull snake.

If, in defending itself, a pit viper stabs rather than bites, only the fangs can come into play; if it actually bites, the two rows of small teeth of the upper jaw and the two of the lower will make their marks in addition to the fangs, which are much farther apart than the rows of teeth. Due allowance must of course be made for bites on finger and toe tips and for those that for various other reasons do not make discernible patterns. Interference by clothing may prevent punctures by the teeth, but it is well known that bites through clothing are not nearly so dangerous as those encountering no such obstruction.

The first demonstrations were made with plasticine cylinders approximately the size of a human wrist. One cylinder, wrapped in a piece of soft, thin paper, was held in front of a rattlesnake, which in turn was lying on the bottom of a large container with sides of wire screening. Figure 3 shows the pattern made by the teeth of a Texas western diamond-back rattler (Crotalus atrox) measuring 39 inches (99 cm.) exclusive of the rattle. Eight teeth of the upper jaw as well as the fangs pierced the paper and entered the plasticine. Five teeth of the right side of the lower jaw made punctures, as did about as many of the left side; some of the impressions made by the teeth of this side were not saparate. Venom that had spilled around the fang punctures was absorbed by the paper, as indicated by stippling in the figure. On each side, about midway between the punctures of the upper and lower jaws, distinct impressions of lip scales could be seen in the plasticine (fig. 3 *B*), showing that a considerable pull must have been exerted by the jaw-closing muscles. Such a bite is not a stab, nor does it leave only the punctures of the two fangs. Figures 1 *A* and 4 show the arrangement of teeth in the western diamond-back rattlesnake and will help any one to understand how a snake with a head only 1 1/16 inches (4 cm.) long can get the teeth of the upper jaw so far from those of the lower. Since the movements of a snake in striking are faster than the human eye, the exact position of the jaws when they are seizing an object is unknown; the figure gives the approximate position only.

The plasticine cylinder was next held in front of the same snake but vertically instead of horizontally, to suggest the position of a leg in walking (fig. 5). The strike produced a pattern differing from the first in only a few points: The marks of the teeth of the upper jaw were a little farther from those of the lower, which indicated that the jaws were spread to their utmost and must have been at about an angle of 180 degrees. The axis of the bite was not vertical; this showed that the snake tilted its head slightly, as if to get a better grip on the almost flat surface confronting it. The marks of the teeth of the lower jaw ran together—proof that the jaw pulled them sharply upward as well as inward. This would be inevitable in a biting rather than a stabbing action. Moreover, the snake bit, in spite of the fact that an

object presenting an almost flat surface would be so much more readily stabbed.

Two cylinders of a plastic called "catabond" were next prepared. At the stage in which it is used, this material is about as resistant to pressure as human flesh. A 27 inch (68.6 cm.) water moccasin (Agkistrodon piscivorus) from Texas was induced to bite this cylinder, with results as shown in figure 6. The water moccasin has more teeth in the upper jaw (five on the palatine bone and fifteen or sixteen on the pterygoid bone on each side), as indicated by the greater number of punctures made in the cylinder. The lower jaw also has more teeth

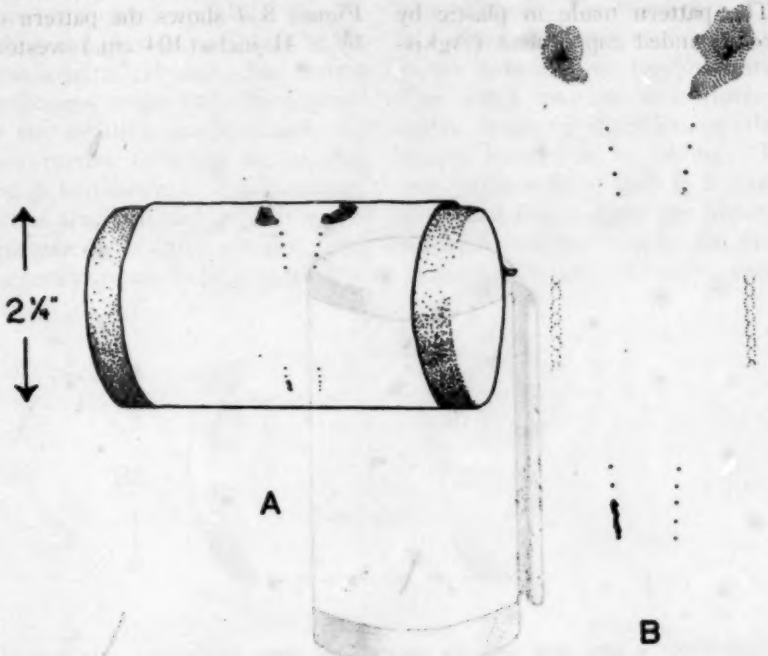

Fig. 3.—Bite pattern of a western diamond-back rattlesnake, made in a plasticine cylinder that was wrapped in thin paper and held horizontally in front of the snake. Stippling represents venom that was spilled on the surface around the fang punctures. On the left side, a replacement fang had become functional before loss of the old fang. In *A*, impressions of the lip scales are outlined by dots. Some of the punctures by the teeth are not separate. *B*, an enlargement of the same pattern flattened and showing in dotted outline impressions that were made through the paper in the plasticine by the lip scales. A few punctures on the lower left side are not separate.

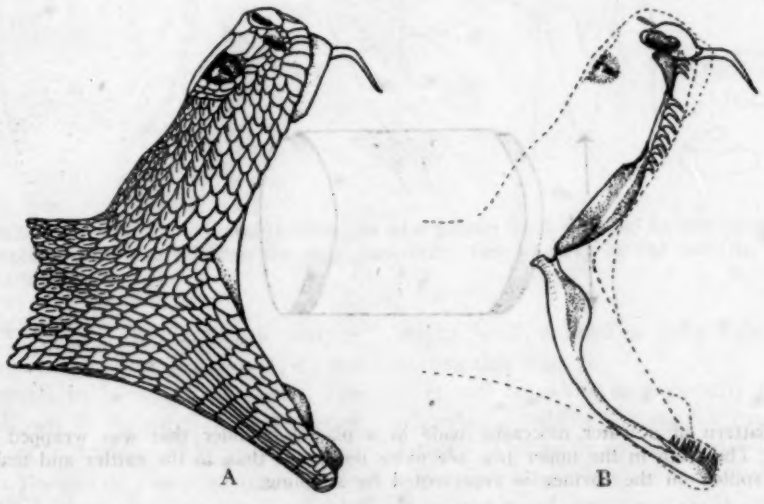

Fig. 4.—*A*, side view of the head of a western diamond-back rattlesnake, with mouth open and fang erect. *B*, phantom view of *A*, showing only the fang on the maxillary bone, the teeth of the upper jaw on the palatine and pterygoid bones and the teeth below on the end of the mandible.

(eighteen). In watching this strike, we got the impression that the snake had to exert considerable effort to free the teeth of the upper jaw from the plastic, by first lifting its fangs. Such would not be the case if it had merely stabbed the cylinder. The pattern made in plastic by the bite of a broad-banded copperhead (Agkistrodon mokasen laticinctus) about 2 feet (61 cm.) long, is shown in figure 7. The number of teeth in the copperhead are: five on the palatine bone and fifteen or sixteen on the pterygoid bone in the upper jaw and fifteen in the lower jaw.

In order to be more realistic, we cast a hand in gelatin and wrapped it with thin paper for use in the next demonstration. The original hand was 7¾ inches (20 cm.) long and 3½ inches (9 cm.) broad (exclusive of the thumb). Figure 8 *A* shows the pattern of a strike made by a 41 inch (104 cm.) western diamond-back rattlesnake when the hand was held at a distance of a few inches, the palm away from the snake and the plane of the hand vertical. The fangs and teeth of the upper jaw caught in the back of the thumb and the teeth of the lower jaw at the base of the back of the index finger.

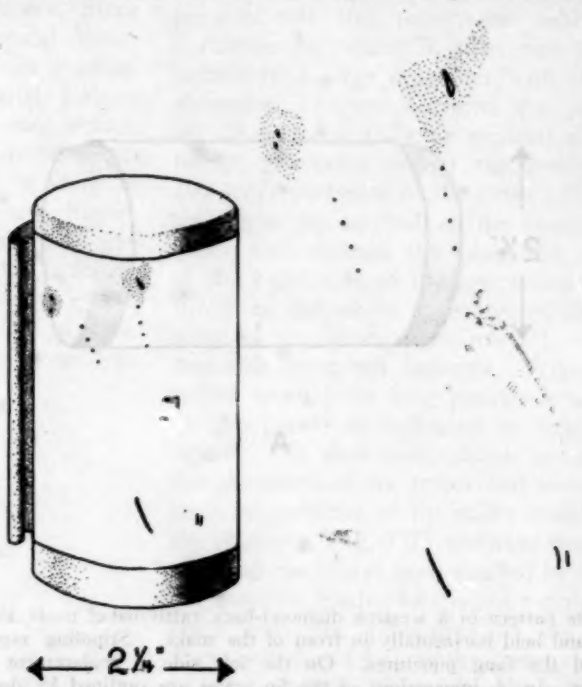

Fig. 5.—Bite pattern made by the same western diamond-back rattlesnake and in the same plasticine cylinder as in figure 3. The cylinder was held vertically, and the snake in biting tilted its jaws somewhat. The punctures of the lower jaw are not discrete, obviously because this jaw was pulled upward. Venom that was spilled on the surface is represented by stippling.

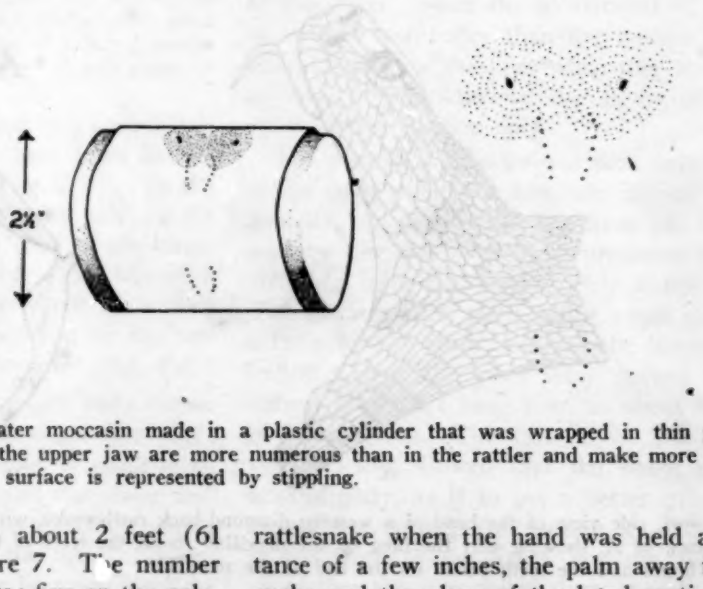

Fig. 6.—Bite pattern of a water moccasin made in a plastic cylinder that was wrapped in thin paper and held horizontally. The teeth in the upper jaw are more numerous than in the rattler and make more punctures. Venom that was spilled on the surface is represented by stippling.

(The marks that almost certainly were made in the gelatin by the teeth of the right upper jaw were indiscernible because of a gap in the paper.) This again shows how wide the jaws stretch. Any one expecting a poisonous snake to make only two punctures would be greatly confused by such a complex wound and might even conclude that a harmless snake had struck or even that a poisonous snake had bitten twice. If convinced of the reptile's potentialities, the victim might have further difficulty in deciding just where the fangs had entered. Perfect interpretation of a bite is accomplished only by working out a clear picture of its pattern. We know of 1 case that greatly puzzled an experienced zoo curator. A large diamond-back rattler struck a keeper's hand, and diagnosis of the tooth pattern proved to be most difficult. The artificial hand, shown in figure 8*B*, was struck from a distance of 6 inches (15 cm.) by our 41 inch (104 cm.) western diamond-back rattlesnake. The strike was directed upward, the fangs and accompanying teeth entering the side of the hand well below the little finger, while the teeth of the lower jaw caught in the palm at a point about on a line with the inner side of the index finger. This stretch is just as great as the preceding one and certainly much wider than any one would imagine such a small snake could achieve.

An effort was made to determine the angle of penetration by the fang, but only a tentative conclusion, and not a new or surprising one, was reached. The basal part of the fangs enters in a plane about perpendicular to that of the roof of the mouth; their tips of course slope inward. The fangs may be withdrawn without appreciably changing direction, or their tips may be moved inward, as in folding. This would indicate incision from each in a direction perpendicular to a line joining the punctures and on the same side of this line as the pricks of the teeth of the upper jaw. As a precaution, the incisions might well extend a relatively short distance across this line.

It will be asked at once why there is so much uncertainty about the marks made by teeth and fangs. The basic reason must be because sufficient emphasis has never been placed on the importance of patterns of the bites. Clothing has no doubt obscured the picture in many cases, and those reported by physicians often have been written up long after the incident, when minor details have faded from the mind. Swelling must also obscure punctures made by teeth, while the action of the venom keeps blood and

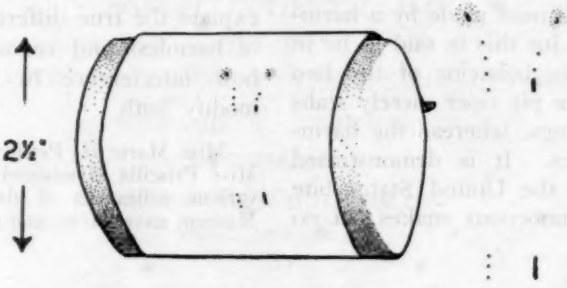

Fig. 7.—Bite pattern of a copperhead made in a plastic cylinder that was wrapped in thin paper and held horizontally. Venom that was spilled on the surface is represented by stippling.

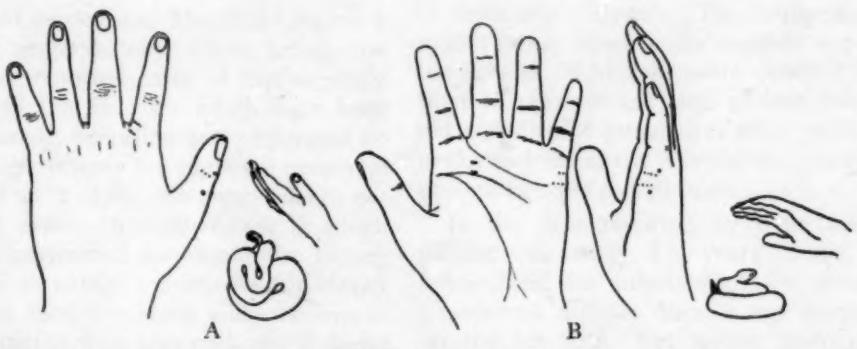

Fig. 8.—Patterns of bites made by a 41 inch rattlesnake in a gelatin hand wrapped in thin paper. In *A* the paper failed to cover completely the area between the fang punctures; hence marks of the teeth in the upper jaw on the right side are lacking.

serum seeping from the fang punctures. No one knows, of course, how many cuts have been made in the wrong place and how many bites by harmless snakes have been cut. There are numerous records of severe symptoms and even death following the bites of innocuous species thought by the victim to be venomous. The introduction of venom causes sharp pain, but an apprehensive person aware of this fact will often imagine pain after the bite of a harmless snake or even after the scratch of a thorn.

SUMMARY

The literature on snake poisoning is misleading in stating that a pit viper in biting makes only one or two large punctures, in contrast to the several rows of small ones made by a harmless snake. The reason for this is said to lie in a difference between the behavior of the two types of snakes; i. e. the pit viper merely stabs with its pair of long fangs, whereas the harmless snake actually bites. It is demonstrated here that pit vipers of the United States bite as effectively as most innocuous snakes; in no sense do they merely stab. The bite pattern of the pit viper, though not simple, can be recognized. Moreover, a careful study of the bite may reveal the approximate location of the pocket of venom, the size of the snake and even its generic identity.

In dealing with any physical injury the first step is to make an exact analysis of it. In the case of snake bite, one must first determine whether one is treating actual snake poisoning or merely superficial scratches and pricks of a harmless snake. Physicians who report cases of poisoning should include diagrams of all marks made by teeth and fangs and thus help in the accumulation of data on bite patterns. Directions for the treatment of snake bite should explain the true difference between the patterns of harmless and venomous snakes and explain how interference by clothing will invariably modify both.

Miss Marie H. Pettibone drew all the illustrations, Miss Priscilla Hannaford gave general assistance and various colleagues of the Chicago Natural History Museum gave advice and technical suggestions.

A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.
LOS ANGELES

FRANK HINMAN, M.D.
SAN FRANCISCO

ALEXANDER von LICHTENBERG, M.D.
MEXICO, MEXICO

ALEXANDER B. HEPLER, M.D.
SEATTLE

ROBERT GUTIERREZ, M.D.
NEW YORK

COMMANDER GERSHOM J. THOMPSON (MC), U.S.N.R.

EDWARD N. COOK, M.D.
ROCHESTER, MINN.

EGON WILDBOLZ, M.D.
BERNE, SWITZERLAND
AND
VINCENT J. O'CONOR, M.D.
CHICAGO

KIDNEY

Anomalies.—Lowsley and Menning[1] report a case of pelvic single kidney, which brings the total number of reported cases of this anomaly to 36. In 13 of the 35 cases which have been reported previously, operation was performed on the kidney. Nephrectomy for supposed neoplasm was performed in 2 cases; obviously, death occurred in both cases. In another case in which operation was performed for tumor the kidney was punctured to obtain a specimen for biopsy and the patient died one week after the operation. Three patients were operated on for stone; 1 died five days after operation. One patient underwent nephrostomy for hydronephrosis. Thus, in 4 of the 13 cases the patients died after operation on the kidney. Most of the earlier deaths are attributable to failure of diagnosis, owing to lack of instrumental and roentgenographic facilities.

The average age of the patients in this series of cases was 25 years. The youngest was an 8 month fetus. Most of the patients were between the ages of 20 and 40 years. Only 1 was more than 47 years of age; this patient was 68 years old and died of pneumonia after pyelotomy was performed for stone. Genital abnormalities were present in 18 of the 36 cases.

In the case reported by these authors, the patient was a boy, 7½ years of age, who was hospitalized for infection of the urinary tract. Cystoscopy did not disclose any ureteral orifice on the left side. Retrograde pyelography disclosed a pelvic kidney lying over the upper portion of the sacrum. The ureter was dilated and tortuous and seemed to terminate abruptly at the intramural portion. A fifteen minute-delayed roentgenogram showed complete retention of the contrast medium. Surgical exposure revealed the ectopic kidney. The ureter was coiled and tortuous, particularly in its upper segments, and was moderately thickened. A metal probe was passed into the ureter. An incision was made over the probe, and the intramural segment of the ureter was dissected free from the bladder. The lumen of the intramural portion of the ureter was definitely stenotic. The kidney was drawn upward, and nephropexy was performed. About

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the writers and are not to be considered as reflecting the policies of the Navy Department.

1. Lowsley, O. S., and Menning, J. H.: Pelvic Single Kidney: Report of a Case, J. Urol. **51**:117-127 (Feb.) 1944.

8 cm. of the redundant ureter was excised. The stump of the ureter was drawn through the opening of the bladder and fastened there. The postoperative course was uneventful. A check-up fifteen months later revealed prompt excretion of the intravenously injected dye. The kidney was in good condition, and there was much less dilatation of the calices than there had been previously.

Culp and Hiebert [2] found congenital anomalies of the ureter in 23, or 3 per cent, of 747 cases in which pyelography was performed because of symptoms referable to the urinary tract. A great variety of anomalous conditions was encountered in this group of 23 cases.

In more than 50 per cent of the cases infection of the urinary tract, lithiasis or hydronephrosis was present. Since all of the patients were comparatively young, there is reason to suspect that secondary pathologic changes eventually may occur in other cases. From the available evidence, one must conclude that anomalous kidneys are more likely to be the site of disease than normally developed kidneys.

In 52.2 per cent of these cases the symptoms were due to secondary pathologic changes. When these changes were eliminated, most of the symptoms were relieved.

Nevertheless, some anomalies appeared to be capable of producing discomfort despite the absence of superimposed disease. This seemed to be true especially in cases of renal ectopia. In almost a third of the cases, however, the symptoms were not related to the anomalies.

Treatment consisted of chemotherapy for infection, ureteral dilatation and surgical removal for calculi and efforts to promote better renal drainage for hydronephrosis. Recurrences of these secondary pathologic changes are to be expected in some instances, and nephrectomy eventually may have to be done in some cases. Congenital anomalies of other systems were present in only 3 cases.

Because of the relatively high incidence of renal symptoms and secondary disease in cases of congenital anomaly of the upper part of the urinary tract, the anomaly must be evaluated cautiously and considered a source of potential urologic difficulty.

Exley and Hotchkiss [3] report a case of clear cell carcinoma of a supernumerary kidney. They say that a true supernumerary kidney, with an individual blood supply and no anatomic connection to another kidney, is extremely rare. This rarity is readily explained when one considers the combination of embryologic circumstances necessary to effect this result. First, there must be an abnormal mesenchymal splitting so that two separate mesenchymal bodies are formed on one side. Then there must be simultaneously and independently a splitting of the ureteral bud as it elongates and migrates cranially on that side.

Forty-three cases of clear cell carcinoma of a supernumerary kidney have been reported, and the case reported by Exley and Hotchkiss makes a total of 44. These authors state:

> The term supernumerary kidney should be reserved for the free accessory organ which is a distinct, encapsulated, large or small parenchymatous mass topographically related to the usual kidney by a loose cellular attachment at most, and often by no attachment whatsoever.

A preoperative diagnosis has been made only 3 times; in many of the cases diagnosis was made at necropsy.

The ages of the patients in the reported cases ranged from 9 months to 67 years. In most of the cases in which operation was performed the symptoms first occurred in the second decade of life, but the condition is prone to produce pathologic change in the kidney in early life. The incidence of the anomaly is equal in the two sexes. The extra kidney may be above or below the normally situated kidney, but it usually is below. Harpster said that the supernumerary kidney may be situated in the iliac region or in the pelvis. In 6 of the reported cases it was in the true pelvis. The supernumerary kidney is also smaller than the normal kidney unless there is an associated disease process.

In the majority of cases the ureters fuse somewhere in their course to the bladder. The most common point of fusion is a short distance above the ureterovesical junction. If there is no fusion of the ureter above the bladder and if cystoscopy reveals a right and left ureteral orifice in the bladder, a careful and diligent search may reveal an extravesical orifice.

In the case reported by Exley and Hotchkiss, the patient was a man, aged 65 years, who complained of general weakness and an uncomfortable feeling in the lower part of his abdomen. Abdominal palpation revealed a movable, firm mass, about 5 inches (12.7 cm.) in diameter, in the middle of the right side of the abdomen. Retrograde pyelography disclosed that the right kidney was comparatively normal; on the right side there were two kidney pelves, which were widely separated, and two separate ureters, which joined

2. Culp, O. S., and Hiebert, P. E.: Clinical Significance of Congenital Anomalies of the Kidney and Ureter, J. Urol. **51**:397-403 (April) 1944.

3. Exley, M., and Hotchkiss, W. S.: Supernumerary Kidney with Clear Cell Carcinoma, J. Urol. **51**:569-578 (June) 1944.

together about midway down their course to the bladder. With the patient under spinal anesthesia, the retroperitoneal region on the right side was explored. A large mass about 5 inches (12.7 cm.) in diameter was present in the lower of the two kidneys on the right side. The two kidneys were completely separate and had separate ureters. The lower kidney, because of its increased growth, had extended down behind the upper kidney. This lower kidney, with its contained mass, was removed. The diagnosis was supernumerary right kidney with carcinoma of the clear cell type.

Nation [4] says that the critical period in fetal life for development of ureteral duplication is the fourth week. Complete ureteral duplication results from the formation of two ureteral buds on one wolffian duct. Partial duplication results from bifurcation or cleavage of the renal pelvis and ureter.

This anomaly was encountered in 0.7 per cent of 16,000 cases in which necropsy was performed. In these cases, the age of the patients who had ureteral duplication did not differ appreciably from the age of other patients. In cases in which the diagnosis is made clinically, renal disease with ureteral duplication is likely to be discovered before middle life.

Ureteral duplication is 27 per cent more common in women than in men. Clinically, this anomaly is observed three times as frequently in women as it is in men. Unilateral ureteral duplication occurs three times as often as bilateral duplication. Unilateral duplication occurs with approximately equal frequency in the right and left ureters and in men and women. Bilateral duplication is approximately 10 per cent more common in women than in men and is observed more often clinically than at necropsy. Ten per cent more of unilateral duplications are incomplete than are complete; the exact reverse is true of bilateral duplications.

Bifurcation occurs with approximately equal frequency in all parts of the ureter. The incidence of renal disease discovered at necropsy is not influenced by ureteral duplication.

The most common pathologic lesions associated with this anomaly are infection, hydronephrosis and nephrolithiasis. The most common symptom is pain. The average blood pressure in this series of cases was lower than that in other cases in which the anomaly was not found at necropsy.

Higbee [5] states that hypoplasia seldom exists alone as a congenital anomaly. Often it is associated with epispadias, hypospadias and pseudohermaphroditism. In the past it has often been overlooked entirely, or if infection has complicated the situation it has been confused with chronic atrophic pyelonephritis.

Renal hypoplasia may be defined as a miniature or rudimentary kidney. It should be differentiated from two closely allied conditions: renal agenesis, in which no renal tissue is present, and renal aplasia, in which rudimentary renal tissue exists without a collecting system.

The distinguishing characteristics of the hypoplastic kidney are: (1) a thin rim of parenchyma usually can be visualized roentgenographically, and (2) it secretes urine of varying quality and amount, which is collected either by normal or bizarre calices or by a hydronephrotic or small bulbous renal pelvis and transferred to the bladder by a well formed ureter. It should also be distinguished from chronic atrophic pyelonephritis. This may be difficult if infection previously has been present. However, the contracted and irregular minor calices will usually stand out, in contrast with those of the congenitally small, smooth, normally formed kidney.

Owing to an unhealthy embryologic background, the hypoplastic kidney is more subject to infection than a normal one and frequently suffers from repeated or chronic infection, which alters the structure of the kidney, both grossly and microscopically. The glomeruli are usually small, though normal. A few may be found hyalinized, and the tubules are lined with low or degenerated epithelium. Some of the tubules that are lined with degenerated epithelium show cystic changes.

Weiss has observed that hypoplastic kidneys are more subject to pyelonephritis than kidneys of normal size and that chronic infection is more likely to persist. Therefore, one might expect an increased incidence of hypertension with infected hypoplastic kidneys. This, however, has not been observed by Higbee. Nephrectomy, when performed, has usually been necessitated in order to relieve either pain or infection. No cases have been encountered in which nephrectomy has been performed with the expectation of curing the accompanying hypertension.

The most common non-nephritic lesions in the order of their decreasing frequency were: (1) atrophic forms of pyelonephritis, including those following previous renal operations, (2) renal

4. Nation, E. F.: Duplication of the Kidney and Ureter: A Statistical Study of Two Hundred and Thirty New Cases, J. Urol. **51**:456-465 (May) 1944.

5. Higbee, D. R.: Congenital Renal Hypoplasia Associated with Hypertension: Report of Two Cases, J. Urol. **51**:466-475 (May) 1944.

neoplasm, (3) renal lithiasis, (4) hydronephrosis, (5) renal tuberculosis and (6) polycystic kidneys.

The best results from operation were obtained in cases of atrophic pyelonephritis with advanced cicatricial changes in the tissues. In 60 per cent of these cases recovery occurred. The second most successful results were obtained in cases of renal tuberculosis associated with hypertension. Recovery occurred in 50 per cent of these cases. Complete recovery occurred in 25 per cent of the cases in which stone and hydronephrosis were associated with hypertension.

Nation [6] states that renal aplasia usually results from failure of proper contact between the ureter and the metanephros. True renal aplasia was found in 16 of 27,000 necropsies. The incidence of the condition in this series was about the same as that of renal agenesia. In 3 cases the anomaly was bilateral. The right and left kidneys were involved with equal frequency. Nine of the patients were males, and 7 were females. Six of the 9 patients who lived more than one month died as a result of hypertension; each had extensive disease of the functioning kidney. Four patients, 3 females and 1 male, had developmental defects of the genital tract. Renal aplasia can seldom be distinguished clinically with certainty from renal agenesia. Operation is indicated for the following conditions: (1) pain, (2) intractable hypertension with no evidence of disease of the functioning kidney and (3) hypertension in which pyelonephritic contracture or renal hypoplasia cannot be excluded.

Tumor.—Herger and Sauer [7] report data on 100 consecutive patients with cortical tumor of the kidney. Seventy-three of the patients were admitted to the hospital with inoperable, recurrent or metastatic lesions, and 27 patients had early or moderately advanced tumors. At the time of the report only 4 patients were alive and apparently well; 11 were alive but still had the disease, 10 could not be traced, 4 had died of other causes and 71 had died of the disease. Operation offers the only chance of cure provided the tumor is still operable. External irradiation is of little or no value in the majority of cases, because parenchymal neoplasms of the kidney are radioresistant. Some of the patients with cortical tumors of the kidney may have symptoms for many years prior to admission to the hospital. These patients may live for a considerable length of time before they succumb to the disease.

Loeb [8] reports a case of Wilms tumor in a woman, 49 years of age, who at the onset had some discomfort in the right flank, which developed into severe pain in the right lumbar region. Bilateral pyelograms showed a normal left kidney, but gross enlargement of the shadow of the right kidney over the upper pole with elongation and distortion of the superior calices. A communicating portion was also filled with the contrast medium. These findings indicated a cystic mass in the upper pole of the right kidney. There was also bilateral calcification of the ligaments connecting the spinal column with the wing of the ilium. A cardiogram was normal. The kidney was removed, and convalescence was uneventful.

Ockerblad and Carlson [9] report a case of Wilms tumor with an eight year cure. The patient was 11 weeks old when first seen. On examination a large mass was found in the left side of the abdomen. A plain roentgenogram and intravenous pyelograms showed normal renal pelvic outlines on the right except for a bifid renal pelvis. On the left side there was no evidence of renal function. A mass occupied the renal region on this side and had displaced the stomach upward and the colon to the right. The left kidney was removed through a subcostal incision. The large tumor mass had replaced the kidney almost entirely. Convalescence was uneventful. The patient was given roentgen therapy for twenty-five days only. Microscopic examination indicated that the growth was a Wilms tumor.

Wood [10] reports a case of Wilms tumor in a Filipino, 45 years of age. The clinical course of the disease from the onset of symptoms lasted seventeen months, the last fourteen of which was spent continuously in the hospital. Histologically, this tumor showed much variation in structure. It consisted of rather well differentiated epithelial structures, resembling abortive tubules and glomeruli, and myoblastic structures, manifesting a lesser degree of differentiation. Some of the metastatic lesions were almost entirely sarcomatous. In such nodules, however, cross striations in the muscle cells could be found only infrequently. Longitudinal myofibrils were more numerous than cross striations. Many of the cells contained "dustlike" cyto-

6. Nation, E. F.: Renal Aplasia: A Study of Sixteen Cases, J. Urol. **51**:579-586 (June) 1944.

7. Herger, C. C., and Sauer, H. R.: Cortical Kidney Tumor—Analysis of One Hundred Consecutive Cases, Surg., Gynec. & Obst. **78**:584-590 (June) 1944.

8. Loeb, M. J.: Report of a Case of Wilms' Tumor in an Adult, J. Urol. **50**:268-273 (Sept.) 1943.

9. Ockerblad, N. F., and Carlson, H. E.: Wilms' Tumor with Report of an Eight-Year Cure, J. Urol. **50**:265-267 (Sept.) 1943.

10. Wood, D. A.: Adenomyosarcoma of the Kidney in the Adult (Wilms' Tumor), J. Urol. **51**:235-244 (March) 1944.

plasmic granules. An accurate diagnosis was not made until completion of studies made at necropsy. Intravenous pyelograms made early in the disease gave uniformly negative results and were noncontributory toward indicating the kidney as a possible source of the disease. The only urinary abnormalities consisted of mild transient hematuria and pyuria at the beginning of the disease. Dull pain in the lumbar region constituted one of the earliest, most persistent and outstanding symptoms.

Melicow [11] reviews 199 cases of renal tumor observed at the Squier Urological Clinic. Nephrectomy was performed in 162 cases. In the majority of the remaining 37 cases the lesion was inoperable. The diagnosis was based on observations made by roentgenography, biopsy or autopsy.

Renal neoplasms are more common in men than in women; the ratio of men to women is 2.5 to 1 (140 men to 59 women).

Neoplasms occur with about equal frequency in the two kidneys. Tumors of the left kidney in Melicow's series predominated in the inoperable group and in the group of highly malignant mixed tumors in both adults (4 on the left to 2 on the right) and infants (6 on the left to 3 on the right).

In 137 cases, or about 70 per cent of the total cases of renal neoplasm, the tumor occurred when the patients were between 41 and 70 years of age. In 69 cases the tumor occurred when the patients were between 51 and 60 years of age. The only tumors encountered in the third decade were relatively benign papillary tumors of the renal pelvis. Half of the mixed tumors in the adults occurred in the fourth decade. All the Wilms tumors in the series (9 cases) were seen before the fifth year.

Painless hematuria was the earliest and most common complaint. From the point of view of the pathologist, it is a late symptom, as it denotes vascular apoplexy due to a well established growth.

The most common symptoms or signs in the order of their frequency were painless hematuria, pain referable to the renal region and a mass. A mass was the presenting symptom in cases in which the tumor was advanced and inoperable. In the majority of these cases, loss of appetite and weight, chills and fever, leukocytosis and secondary anemia were also present.

In cases of tumor of the renal pelvis, a constant filling defect observed in repeated pyelograms was suggestive. In cases of early clear cell carcinoma the characteristic pyelogram showed elongated thinned calices. In cases of more advanced tumor and granular cell carcinoma and mixed tumor, there were in addition, distortion and obliteration of some or of all the calices. Scattered dots of calcium were suggestive of deposits of lime in an old hemorrhage within a tumor or cyst or both and were usually found in lesions of long standing.

The papillary pelvic tumors tended to grow slowly, and those which were relatively benign occurred in the younger age groups (third decade). Some grew along the ureter and into the bladder. In a number of cases the tendency for subsequent development of papillary neoplasms in the ureter, bladder and urethra was suggestive of a neoplastogenic proclivity of the epithelium of the entire urinary tract.

The nonpapillary pelvic tumors were of the metaplastic squamous cell variety with "epithelial pearl" formation. They tended to become ulcerated and covered with calcareous debris or calculi. They usually invaded the kidney. Fever and leukocytosis were present.

Parenchymal tumors occurred in any portion of the kidney and grew in all directions. Those near the pelvis tended to invade it and the hilar structures. Those near the renal capsule tended to grow through it into neighboring tissues. The larger and heavier the tumor, the worse, as a rule, was the end result. When gross breaking of barriers or hemorrhage was found, local invasiveness and distant metastasis were likely.

The so-called Grawitz tumors, or hypernephromas, were usually clear cell carcinomas arising apparently from the epithelium of the tubules or from clear cell adenomas. They were yellowish and circumscribed. True hypernephromas, of adrenal rest origin, were rare.

The so-called hypernephroid carcinomas were usually granular cell carcinomas or adenocarcinomas arising apparently from the epithelium of Bowman's capsules or of the glomerular tufts or from the granular cell adenomas. They were grayish, infiltrating and devoid of a capsule.

The mixed tumors of the kidney in adults were usually carcinomatous centrally and sarcomatous peripherally. This probably was indicative of a highly active metaplasia or anaplasia. The mixed tumors in infants were usually carcinosarcomas and were apparently of dual origin.

It was at times impossible to distinguish microscopically a papillary carcinoma of the pelvis which had diffusely invaded the kidney from a clear cell carcinoma with papillary formation of

11. Melicow, M. M.: Classification of Renal Neoplasms: A Clinical and Pathological Study Based on One Hundred and Ninety-Nine Cases, J. Urol. **51**: 333-385 (April) 1944.

similar invasiveness, from a granular cell carcinoma involving the entire parenchyma or from a papillary cyst carcinoma which had penetrated the capsule and spread out.

Multiple adenomas, multiple cystadenomas or multiple papillary cystadenomas were usually secondary findings in a sclerotic kidney. The bilateral nature of the disease in some of the cases was suggested by the postoperative course and proved by autopsy.

The grading of renal tumors, except those arising in the pelvis, is not feasible. Amitosis is the rule. Prognosis depends on the duration of symptoms (the longer, the worse), the character of the presenting symptoms (the presence of the three most common symptoms or their reversal is a bad omen) and the size of the tumor (the larger and heavier tumors are usually more malignant). Other adverse factors are the breaking of gross and microscopic barriers and the presence of hemorrhage and secondary changes.

The prognosis for parenchymal tumors is progressively worse from: (*a*) the uncomplicated single nodule of clear cell carcinoma to (*b*) the multiple nodules of clear cell carcinoma with hemorrhages to (*c*) the granular cell carcinoma to (*d*) the mixed cell tumor.

The advent of metastasis is a matter of lymphatic or vascular penetration by tumor cells. While the incidence for local recurrence and metastasis increases progressively in the foregoing groups, nevertheless occasionally a small clear cell carcinoma, usually near the hilar region, may metastasize early, while a huge cystic mass containing tumor may remain sharply localized for a long time.

Rottino and Mohan [12] report 3 cases of hemangioma of the kidney. In 2 of the cases diagnosis was made when nephrectomy was performed, and in the third case it was made at necropsy. The first 2 cases comprise the only instances of renal hemangioma in 169 cases in which nephrectomy was performed in ten years at St. Vincent's Hospital (New York). The third case comprises the only instance of renal hemangioma in 1,650 cases in which necropsy was performed. Riley and Swan did not find a single case of this tumor in 13,219 cases in which necropsy was performed at the Boston City Hospital. Study of removed kidneys impressed Rottino and Mohan with the insignificant size of hemangiomas and with their obscure situation. Their true nature was realized only after careful microscopic study. This fact makes questionable the presumed rarity of renal hemangioma. Indeed, in the absence of hematuria many of these tumors must pass unnoticed.

Shaheen, Cassano and Lisa [13] review 30 cases of primary carcinoma of the kidney in which necropsy was performed. These cases comprise about a fourth of all the instances of primary renal tumor found in 5,100 autopsies. Primary renal tumor was more frequent among males than females. It usually occurred beyond the sixtieth year of life. The clinical triad of hematuria, pain and palpable tumor occurred in about a sixth of the cases. In about an equal number of cases, the tumor mass was the only clinical sign. The presenting symptoms were as frequently caused by metastatic or embolic processes as they were by genitourinary disturbances. In a fourth of the cases, the malignant lesion was unrelated to the clinical disease or to the cause of death. Retrograde pyelography was the most valuable of the diagnostic laboratory procedures. Carcinoma of the kidney is of renal origin and does not originate from adrenal rests.

Trauma.—Adlington [14] reports a case of traumatic rupture of the kidney and spleen with dislocated pelvis. The patient, a man aged 36 years, had a severe accident in a steel mill. Directly after his hospitalization, there was severe abdominal pain, which caused vomiting. The preoperative diagnosis was ruptured left kidney with intraperitoneal hemorrhage. A catheterized specimen of urine contained some blood. Exploratory operation disclosed a large rent in the peritoneum of the left paracolic gutter, and a small pyramidal-shaped piece of kidney was mopped out of the peritoneal cavity. The kidney was severely lacerated and was removed. The bleeding still continued, and palpation of the spleen revealed severe laceration of this organ. The spleen was then removed and the abdomen closed. The patient recovered from the operation; he could walk well and was free of pain before his dismissal from the hospital. Desjaques and others (1930) reported nearly a 50 per cent recovery rate with combined nephrectomy and splenectomy in 46 cases of concomitant rupture of the spleen and the left kidney.

Meltzer,[15] in searching the literature, found reports of 18 authentic cases of true traumatic hydronephrosis. He reports a case of giant-sized hydronephrosis, which illustrates the importance

12. Rottino, A., and Mohan, H.: Renal Hemangioma: An Obscure Cause of Hematuria, J. Urol. **51**:601-605 (June) 1944.

13. Shaheen, A. L.; Cassano, C., and Lisa, J. R.: Primary Tumors of the Kidney, J. Urol. **51**:597-600 (June) 1944.

14. Adlington, S. R.: Traumatic Rupture of Kidney and Spleen, with Dislocated Pelvis, Brit. J. Surg. **31**: 407-408 (April) 1944.

15. Meltzer, M.: Giant Hydronephrosis Following Generalized Trauma, J. Urol. **51**:491-495 (May) 1944.

of carrying out urologic examination when there is a history of an old injury to the abdomen or the back. Months or years later the only subjective symptoms may be vague and mild backache, abdominal pain or a sense of fulness and weight in the abdomen, with or without urinary symptoms. A large hydronephrotic sac may be present for some time, and yet the patient may have no discomfort or localizing pain.

Stone.—Thompson, Steadman, Benjamin and Scott [16] made a quantitative chemical analysis of 47 human urinary calculi, which revealed that 78 per cent were of the calcium oxalate-phosphate type, 16 per cent contained magnesium as a significant component, either alone or in combination with a calcium phosphate, and 6 per cent were composed predominantly of uric acid.

Evidence has been cited to indicate that among calculi of the oxalate-phosphate type, the heavier calculi contain more phosphate, while those of lighter weight are relatively richer in oxalate. The variation in proportion of oxalate to phosphate is without significant effect on the percentage of calcium, which is nearly constant at about 25 per cent. This finding does not hold for the three component stones. Small amounts of nitrogen from an unidentified source are consistently found, and the percentage of this is unrelated to the weight of the calculus. The general observation that urinary calculi consist predominantly of more than one component has been confirmed.

Quantitative spectrochemical analyses made on 1 mg. samples of the stones verified the principal findings of the chemical analyses and, in addition, showed the occasional presence of traces of other common elements, such as lead, copper, manganese, silver, bismuth and sodium.

Infection was more frequently associated with magnesium ammonium phosphate stones than with calcium oxalate–phosphate calculi.

No relationship was found between the type of infection and the chemical constitution of the renal calculi analyzed.

In selected cases, no vitamin A deficiency was found.

Farman [17] reports a case of bilateral nephrolithiasis in a horseshoe kidney. A man, aged 36 years, complained primarily of backache. A roentgenogram showed extensive bilateral nephrolithiasis. Pyelograms revealed that the right renal pelvis was completely filled with a large stone, that there was an impassable obstruction of the upper part of the left ureter and that multiple calculi were scattered throughout the left renal area. A left anterior pyelolithotomy and nephrostomy were performed, and 38 stones were removed. One month later, a right pyelolithotomy and nephrostomy were performed. Cystoscopy, done three weeks later, revealed that both ureters were open.

Farman states that factors influencing the formation of calculi are more frequently evident within the fused (anomalous) kidney than in the normally formed kidney. In reported cases, a calculus has been the most commonly found concomitant lesion. Extreme caution, full knowledge of anatomic relationship and great appreciation of operative and clinical hazards should motivate all approach to surgical correction of the anomalous or fused type of kidney and associated pathologic changes.

Rickets.—Hayward [18] discusses the syndrome known as renal rickets. As the title implies, rachitic changes are present. They are assumed to be caused by renal dysfunction. The syndrome is found among young persons; the average age of patients at the time of onset of symptoms is 12½ years. Hayward describes a typical case.

The following signs and symptoms may be noted before the patient is 13 years of age: The average height is 24.2 per cent below normal, and the average weight is 45.2 per cent below normal. Signs and symptoms may or may not lead to an examination of the urinary tract. Mentality is good. Bony changes develop; genu valgum or knock knees are present in 56 per cent of the cases. Other bony changes are less constant. The roentgenographic findings are typical of ordinary rickets. Thirst, polyuria, dryness of skin, loss of appetite, headache and delayed sexual development are present, depending on the severity of the renal involvement. Laboratory studies show poor renal function, azotemia and, most important of all, a reversal of the calcium-phosphorus ratio. Of the preceding symptoms, the three outstanding diagnostic points are dwarfism, rachitic changes and reversal of the calcium-phosphorus ratio.

The type of renal impairment is unimportant. Obstruction of the urinary tract, nephritis, congenital cystic disease or other changes can initiate the train of events. Practically all contributors on the subject agree on one thing, namely that the kidney is unable to excrete phosphorus. This accounts for the high value

16. Thompson, H. E.; Steadman, L. T.; Benjamin, J. A., and Scott, W. W.: Quantitative Microchemical and Spectrographic Data on Renal Calculi and Their Relation to Infection, J. Urol. **51**:259-271 (March) 1944.

17. Farman F.: Bilateral Nephrolithiasis in Horseshoe Kidney, J. Urol. **51**:447-455 (May) 1944.

18. Hayward, W. G.: The Renal Rickets Syndrome, J. Urol. **51**:278-286 (March) 1944.

for the serum phosphorus. The phosphorus is eliminated into the bowel, where it combines with calcium to form insoluble calcium phosphate, which the bowel cannot absorb. As a result, a calcium deficiency occurs.

Not only is exogenous calcium prevented from entering the system, but endogenous calcium is being removed by parathyroid action.

The daily requirement of calcium during growth is from 0.4 to 1 Gm. or more. Calcium phosphate comprises 80 per cent of bone. Bone is the reservoir of both calcium and phosphorus, and these are constantly being added to or drawn from bone. Acidosis, which is present with this syndrome, ionizes enough free calcium to keep its level above 3.8 Gm.

Any renal lesion so severe as to cause failure of excretion of phosphorus may be present. Albright and others stated that parathyroid cells are not as large in this type of hyperparathyroidism as they are in primary hyperparathyroidism. As for bony changes, Albright and his co-workers clearly explained that they are due to secondary hyperparathyroidism and consist of swollen metaphyses, bony replacement with fibrous tissue, cysts and hemorrhage. Genu valgum, deformity of the thorax, rachitic rosary, a wooly appearance of the skull and fractures may be present.

The symptoms associated with lowered renal function vary, as would be expected, and consist of headache, anorexia, nausea, vomiting and increased thirst. In several of the cases reported in the literature the stature remained small and there was no bony deformity until adolescence, when the patients began to grow rapidly. Genu valgum developed at this time.

The syndrome rarely can be treated successfully. It may be postulated that if treatment is to be successful the renal lesion must be of the obstructive type and the patient must be seen before irreparable renal damage has occurred.

It is obvious that nephritis severe enough to cause this syndrome must offer a poor prognosis, as must polycystic disease. The seriousness of this condition can best be brought home by stating that necropsy was performed in almost all of the comparatively large number of cases reviewed. The duration of life is almost two years after bony changes occur.

Infection.—Munger [19] says that cortical abscesses and renal carbuncles are distinct pathologic and clinical entities. These conditions frequently are difficult to diagnose. A careful study of the history, with inquiry into antecedent superficial infection, and of the physical and roentgenologic findings usually will enable one to make a correct diagnosis. Adequate incision, decapsulation and drainage usually are curative. The sulfonamide drugs are definite adjuncts.

Function.—Baumrucker [20] found that after the injection of contrast substances for excretion pyelography the specific gravity of the urine increases in proportion to the concentration of the dye. There is a close parallel between visualization of the kidney and increase in the specific gravity of the urine after the injection of diodrast solution. This increase in specific gravity allows computation of the amount and percentage of dye excreted. The author has devised an equation for calculating renal function. While excretory pyelography enables one to determine the concentrating ability of the kidney, the equation supplies the numerical equivalent, or the percentage of the contrast medium excreted. In pyelograms, kidneys that are unable to concentrate urine sufficiently to cause an added rise in the specific gravity of the excreted urine of 0.018 (as from 1.024 to 1.042) after injection of diodrast solution usually will not appear as clearly as will kidneys that are able to effect such a concentration. Good pyelograms are dependent on the preparation of the patient and on the pyelographic technic. To the factors of dehydration and evacuation may be added a third, namely gravity. The author has modified the customary technic by placing the patient in a Trendelenburg position of 25 to 30 degrees. This facilitates filling of the renal pelvis and hence permits better visualization of the kidneys.

Thrombosis.—Melick and Vitt [21] report a case of thrombosis of the renal vein. The patient was a woman, aged 33 years, who complained of chills, fever and pain in the right side of the thorax and back. Cystoscopy revealed that the bladder was normal but that no urine came from the right ureter. Ureteral catheters were passed on both sides without difficulty. There was no drainage on the right side. The right renal pelvis was poorly visualized and irregular in outline in retrograde pyelograms; the left kidney was normal. Exploratory operation revealed that the right kidney was considerably larger than normal. Palpation of the pedicle revealed thrombosis of the renal vein. The kidney was removed.

In adults thrombosis of the renal vein may be due to primary hematogenous pyelonephritis, with resultant thrombosis within the renal cortex and extension to the pedicle. It also may be

19. Munger, A. D.: General Aspects of Acute Surgical Infections of the Kidney, South. M. J. **37**: 20-23 (Jan.) 1944.

20. Baumrucker, G. O.: Estimation of Renal Function Based on Specific Gravity Changes Following Intravenous Urography, J. Urol. **50**:290-300 (Sept.) 1943.

21. Melick, W. F., and Vitt, A. E.: Thrombosis of the Renal Vein. I. Urol. **51**:587-596 (June) 1944.

due to involvement of the pedicle by infection, from rupture of either a cortical abscess or a perinephritic abscess. The thrombosis of the renal vein may be part of a progressive, ascending inflammatory process involving, first, the vessels of the pelvis or lower extremity and, then, the inferior vena cava and its higher branches. In infants, the thrombosis is almost always secondary to severe ileocolitis or gastrointestinal upsets. In 1 infant, the thrombosis was secondary to primary pneumonitis.

The onset is usually sudden; there are fever, pain and tenderness on the affected side. On palpation, the kidney has been found to be enlarged in every case reported so far. The kidney is also freely movable and extremely tender. Usually there are signs of infection and severe toxemia. Frank hematuria or microscopic hematuria has been present in almost every case.

Surgical removal of the kidney seems to be the treatment of choice. Nephrectomy or attempted nephrectomy was employed in 14 cases of thrombosis of the renal vein. Ten patients recovered, and 4 died. However, in cases in which operation was not performed, no patients recovered although some lived for several months. The operation seems to be more successful the earlier it is performed. Campbell and Matthews found an abnormally prolonged prothrombin time in 2 infants. For this reason they stressed the importance of administration of vitamin K. For adults it would seem more rational to use substances such as heparin or dicoumarin to prolong the prothrombin time and prevent, if possible, further extension of the thrombotic process.

Diagnostic Value of Overdistention of the Renal Pelvis.—Wattenberg and Rose [22] found that overdistending the renal pelvis with fluid through a ureteral catheter will produce pain unless the pelvis previously has been subjected to back pressure of some degree for a long time. Such back pressure causes desensitization, that is, it is a process of physiologic adaptation. Pain arising in the renal pelvis often is referred atypically. Such referred pain cannot be reproduced, but the central pain can be reproduced. Nonirritating fluids should be used, water preferably. Irritating fluids cause generalized ureteral spasm and cloud the picture. Reproducing ureteral pain by passing a ureteral catheter is not a reliable test, although it may be of value at times. A blocked pelvic or ureteral muscle goes through stages of compensation (irritability and hyperplasia) and decompensation (desensitization and overstretching). Generally, however, with exceptions, colicky and intermittent pain is associated with the hyperirritable stages, and dull, heavy costovertebral pain is associated with a dilated renal pelvis. The patient must state that the overdistention is accurately reproducing his pain; otherwise, the test is of doubtful value. Wattenberg and Rose have found the test nearly 100 per cent accurate when considered with the preceding exceptions. It frequently indicates the subsequent treatment.

Operations and Postoperative Complications.—Flo and Cummings [23] report a case in which unilateral decapsulation of the kidney was performed for transfusion oliguria. The patient was a woman, aged 48 years, who after transfusion had a greatly decreased urinary output and a concentration of 118 mg. of nonprotein nitrogen per hundred cubic centimeters of blood. As she was in poor general condition, a unilateral decapsulation only was done. She seemed considerably better immediately after operation. Her vomiting ceased, and she was more alert. Intravenous administration of fluid was continued, and urinary secretion commenced at once. The first twenty-four hour period produced 211 cc. of urine and the second 625 cc.

Flo and Cummings state that the exact mechanism is not clearly understood but deserves investigation; if unilateral decapsulation will break the vicious chain of events, it is the procedure of choice.

Wilhelm,[24] in discussing reimplantation of the renal pelvis, states that the most favorable results have been observed after the Y plastic or the side to side anastomosis, which preserves the physical continuity of the pelvis and ureter. Sometimes, however, this type of operation is not feasible because of shortness of the ureter, as in cases of traumatic avulsion or extensive stricture. In this event, an end to end anastomosis is made between the sectioned ureter and the pelvis.

In a review of 11 cases in which the ureter was reimplanted into the renal pelvis, 7 instances of partial or complete occlusion at the site of anastomosis a short time after operation were found. The anatomic cause of obstruction was determined in 3 of these cases.

With the recognition that simple end to end anastomosis over a splinting catheter is likely to result in loss of continuity or in stricture, various technics have been suggested in an attempt to

22. Wattenberg, C. A., and Rose, D. K.: Reproduction of Renal Overdistention Pain: Its Clinical Diagnostic Value, J. Urol. **50**:280-289 (Sept.) 1943.

23. Flo, S. C., and Cummings, H. W.: Unilateral Decapsulation of Kidney for Transfusion Oliguria, Surgery **14**:216-222 (Aug.) 1943.

24. Wilhelm, S. F.: Reimplantation of the Renal Pelvis, J. Urol. **50**:274-277 (Sept.) 1943.

insure patency of the stoma. Most practical of these is splitting the upper end of the ureter for 1 cm. into two straps. The ureter is then implanted into the pelvis and the straps sutured to its inner surface. A splinting catheter and a nephrostomy tube are left in place. The ureteral straps, however, may become loose and form an occluding rosette or valve, which will interfere with the downward flow of urine.

In order to prevent the formation of an obstructive valve, a technic was planned in which the renal pelvis is implanted into the ureter. The upper end of the ureter is split for 1 cm. into two straps. These straps are placed and sutured outside the renal pelvis. The anastomosis is made over a splinting catheter, and nephrostomy and nephropexy also are performed. If the externally sutured ureteral straps should loosen, they would not obstruct the newly made stoma.

Wilhelm reports a case in which a man 51 years old entered the hospital on July 2, 1942 for removal of 4 calculi from the left kidney. At operation, the ureter was found embedded in thick, infiltrated fat and adhesions; it was sectioned transversely. Four calculi were removed from the renal pelvis and calices, and a Malecot nephrostomy tube and a Garceau catheter were inserted through the renal cortex into the pelvis. The upper end of the ureter was split into two straps, each 1 cm. in length. The Garceau catheter was then passed down the ureter for 12 cm. and acted as a splint. The renal pelvis was reimplanted into the ureter, and the ureteral straps were sutured to the external surface of the pelvis by four interrupted sutures of fine chromic surgical gut. A nephropexy was done.

After removal of the splinting Garceau catheter on the twenty-fourth postoperative day, indigo carmine was injected into the nephrostomy tube and appeared promptly in the vesical urine. On the twenty-ninth postoperative day, the nephrostomy tube was clamped off. The wound remained dry for the next six days, and there were no untoward symptoms. The tube was removed on the thirty-fifth postoperative day, and within seventy-two hours the sinus was closed and dry. The patient left the hospital on the following day and has been well since that time. The wound remained healed. On September 10, an excretory urogram revealed fair function in both kidneys and slight dilatation of the pelvis of the left kidney. A left retrograde pyeloureterogram also showed some dilatation of the renal pelvis. Although the site of anastomosis was marked by an indentation, the stoma was widely patent and there was no retention of the contrast medium.

Caughlan and Boler [25] discussed the value of two stage nephrectomy. They deliberately planned and carried out two stage nephrectomy on several patients and found that it was much less hazardous than single stage nephrectomy.

One patient had a tumor of the left kidney. The kidney was exposed at the first operation, and four days later it was removed.

The second patient was a girl, aged 14 years, who had a large Wilms tumor of the kidney. She was given roentgen therapy and supportive therapy before operation. A two stage nephrectomy was done transperitoneally. At the first stage, the kidney was exposed and the vascular pedicle ligated. At the second stage, twenty-four hours later, the original incision was opened, the pedicle religated and the kidney removed in a short time.

Caughlan and Boler state that in their opinion both of these patients would have died had the operation been carried out in one stage. They suggest that two stage nephrectomy might be carried out in cases of pyonephrosis or renal tuberculosis or in any case in which nephrectomy would require a long time.

Hayward [26] presents a case in which hypertension developed promptly after a plastic operation on a hydronephrotic kidney. The blood pressure immediately returned to normal after removal of the kidney. It is reasonable to believe, and it is borne out in practice, that the more promptly unilateral nephrectomy is performed in selected cases after the advent of hypertension, the better the chance of cure. In a large number of cases in which conservative renal operations are performed, the kidney becomes fixed in scar tissue. This may cause renal ischemia by pressure on the parenchyma or by compression on the pedicle. Blood pressure should be carefully watched after conservative operations on the kidney.

Lazarus [27] states that gas bacillus infection complicating operation on the upper part of the urinary tract is rare. Only 25 cases of this complication have been reported, including the 2 reported by him. Although gas bacillus infection may be due to a variety of organisms, the predominating one is Bacillus welchii.

While the usual incubation period varies from one to six days, the average being three days, the infection has been known to occur as soon

25. Caughlan, G. V., and Boler, T. D.: Two-Stage Nephrectomy, J. Urol. **51**:481-485 (May) 1944.

26. Hayward, W. G.: Renal Surgery as a Cause of Renal Ischemia, J. Urol. **51**:486-490 (May) 1944.

27. Lazarus, J. A.: Bacillus Welchii Infections Complicating Surgical Procedures upon the Upper Urinary Tract, J. Urol. **51**:315-324 (March) 1944.

as a few hours after operation and as long as ten years after inoculation. The outstanding clinical features of this infection are rise in temperature and pulse rate, severe toxemia, edema and pain in the wound and typical purplish discoloration of the surrounding skin, followed later by coalescing blebs. The diagnostic features are crepitation in the subcutaneous tissues and serosanguineous discharge, with a typical sweetish, mousy odor. Smears and cultures will disclose Bacillus welchii. Smears may be positive within six hours and cultures within four hours after the onset of infection.

Treatment consists of wide open drainage and generous use of oxygenized antiseptic solutions, along with polyvalent Bacillus perfringens serum. Judging from the cases reported by Lazarus, it appears possible that sulfonamide drugs administered locally and orally are coming to play an important role in the prophylaxis and actual treatment of this type of infection. Roentgen therapy has been advocated in the early stages of the disease. In the reported cases, 71.4 per cent of the patients recovered. Of the patients who recovered, 73.3 per cent received serum. Of the 6 patients who died, 2 died before any treatment could be given and the remaining 4 received serum.

The kidney was the source of infection in 23 (92 per cent) of the 25 cases reported, and the ureter was the source of infection in 2 cases (8 per cent). The following operations preceded the infection: nephrectomy in 45.4 per cent, nephrotomy in 18.1 per cent and pyelotomy in 22.7 per cent of the cases respectively. Calculi were present in 15 (60 per cent) of the cases; renal calculi were present in all 15 and ureteral calculi in 2. In 6 of these 15 cases pyonephrosis also was present. Renal infection necessitating nephrectomy was present in 11 cases (44 per cent), and in 5 cases the infection was associated with calculi.

In the first of the 2 cases reported by Lazarus, a fulminating infection followed the removal of multiple calculi, one of which was fragmented. Clinical evidence of infection appeared seven hours after operation. In the second case, pyelolithotomy was performed for a single calculus which was not fragmented. In this case, sulfadiazine had been administered because of pulmonary involvement immediately after the operation. The first indication of infection of the wound occurred forty-eight hours after operation.

In view of the fact that the opening in the renal pelvis was not sutured after removal of the calculus and since the calculus was removed intact, it is extremely likely that the escape of infected urine from the kidney into the wound played an important role in the development of this complication. For this reason, it is suggested that in cases of renal or ureteral calculi openings made in the ureter or renal pelvis should be closed tightly, particularly if the calculi are accompanied by urinary infection.

Schneider [28] reports a case of postnephrectomy duodenal fistula with recovery, along with 3 additional cases in which the patients died. Two cases in which a fecal fistula occurred after removal of the right kidney is reported to show that this complication also may occur. Treatment of the duodenal fistula may be: (*a*) conservative, which may be systemic and local, or (*b*) radical, either immediate or late, depending on the patient and the surgeon. Schneider concluded that if the meager figures presented are any indication at all there is practically no difference between the results of conservative and radical treatment, the mortality being about the same for both. Complications may sometimes be avoided by performing subcapsular instead of extracapsular nephrectomy.

Taylor and Taylor [29] report a case in which duodenal fistula followed nephrectomy. The patient was a man, aged 30 years, who had had an operation on the left kidney for the removal of stones. Three weeks later an operation had been performed on the right kidney for the same reason. Several months later reexamination revealed good function in the left kidney, but no function in the right kidney. A short time later a bulging abscess was found in the region of the right kidney. The abscess was drained. Six months later the right kidney was removed. The kidney was adherent to all surrounding structures. Three days after the operation, a slight greenish tinge was noticed in the drainage from the wound. The drainage increased, and it evidently came from the duodenum. The wound was protected, and owing to the basic condition no effort was made to close the fistula, which continued to drain for forty days and finally healed.

28. Schneider, D. H.: Duodenal Fistula After Kidney Surgery, J. Urol. **51**:287-295 (March) 1944.

29. Taylor, C. B., and Taylor, J. M.: Duodenal Fistula Following Nephrectomy: Case Report, J. Urol. **50**:278-279 (Sept.) 1943.

(To Be Concluded)

PROGRESS IN ORTHOPEDIC SURGERY FOR 1943

A REVIEW PREPARED BY AN EDITORIAL BOARD OF THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS

XII. CONDITIONS INVOLVING THE FOOT AND ANKLE

PREPARED BY EMIL D. W. HAUSER, M.D., CHICAGO, AND ROBERT P. MONTGOMERY, M.D., MILWAUKEE

Stevenson [434] gives a review of the common disorders of the foot that cause disability in the army. The most important are those due to static changes, but he also brings out some of those due to rare tropical diseases. The importance of vascular changes as well as the occurrence and treatment of dermatomycosis is included. The treatment of common injuries, such as sprains and puncture wounds, is clearly presented.

Dredge [435] takes up the common disabilities of the foot that occur in the army and groups them into four classifications: the traumatic, the mechanical static, the occupational, which include vascular disturbances, and the dermatologic, principally trichophytosis. The treatment for the disabilities is classified and does not materially vary from the accepted methods.

Fripp [436] brings out the fact that chronic and acute foot strain are not specifically wartime disabilities, but an army marches and a nation works largely on its feet, so that if there are any predisposing factors the increased strain of war work may cause a partial or complete breakdown. In the treatment of chronic foot strain he uses physical therapy methods, and for acute foot strain he emphasizes the need of rest and then heat and massage and faradic stimulation. If there is persistence of pain he uses an injection of 2 per cent solution of procaine hydrochloride.

The article also includes the treatment of crush injuries, lacerations and compound fractures. Immediate excision of the cutaneous edges is recommended. Primary closure should be attempted only if operation is carried out within eight hours after injury and if the cutaneous edges can be brought together without tension. In his opinion, repeated application of closed plaster casts is the accepted method of after-treatment. For fractures he recommends the unpadded, closed plaster cast and warns of the danger of interference with circulation. He advises the sparing use of narcotics, so as not to mask the danger signs in the first twenty-four hours.

[ED. NOTE.—The after-treatment of open wounds by means of a closed cast is still a question. The difference of opinion is primarily due to the different circumstances surrounding the cases. In the African campaign the open method was proved to be the method of choice, whereas in the Russian campaign the circumstances were such that the closed method was preferable. These circumstances include the comparative organization of transportation facilities for immediate care as well as the type and number of bacteria that may be encountered.]

Lake [437] notes a vicious circle of "foot strain as a factor producing fatigue in industry and the Services" and "industry and the Services as factors producing foot strain and fatigue." He suggests that foot strain can be prevented by keeping the weight distributed as it should be and by avoiding undue continuous strain on the connective tissues, particularly the ligaments and fascia of the sole. The problem of foot strain in the services is different, for here the foot breaks down as a result of excessive activity and movement. Suddenness of change to military life is a factor. He advises more gradual methods of training. He points out that the problem of foot fatigue is complicated, demanding study of each case individually; no stereotyped measures can be expected to constitute a shortcut to relief.

Hellebrandt, Nelson and Larsen [438] have made a study to determine whether there is significant

434. Stevenson, A. S.: The Management of Disabilities of the Feet in the Army, M. Clin. North America **27**: 1129-1153 (July) 1943.

435. Dredge, T. E.: Physical Treatment of Disabilities of Foot Commonly Encountered in Military Service, Arch. Phys. Therapy **24**:653-659 (Nov.) 1943.

436. Fripp, A. T.: Some Common Wartime Disabilities of Feet, M. Press **208**:347-350 (Nov. 25) 1942.

437. Lake, N. C.: Foot as Factor Producing Fatigue in Industry and the Services, M. Press **208**:344-347 (Nov. 25) 1942.

438. Hellebrandt, F. A.; Nelson, B. G., and Larsen, E. M.: The Eccentricity of Standing and Its Cause, Am. J. Physiol. **140**:205-211 (Nov.) 1943.

antecedence for the volitional use and the difference in strength and size of the limbs of the two sides of the body. Their study was conducted first to find out if there was a preference for either limb. They repeated the method of Irwin and corroborated his findings. They also tested the strength and then measured the volume of the limbs by submerging them in fluid and measuring the displacement. They measured the morphologic symmetry by balancing the body on a movable platform suspended from the edges of knives. The result of their experiment shows that there is a slight preponderance of choice for the right foot in the preference test. They arrived at the following conclusions from their evidence: Morphologic and functional asymmetries occur in limb preference, volume and strength. Although most of the observed asymmetries are too small to have statistical significance, they constantly favor the right side. It is suggested that in the aggregate these small dextral asymmetries in functional capacity associated with like differences in strength and size have the effect of a slightly eccentric counterweight on the incessantly shifting rotatory movements acting on the joints of the weight-bearing skeletal parts.

[Ed. Note.—This scientific investigation may lead to some clinical significance. In our clinical experience the left foot gives more trouble than the right. The significance of their findings in relation to our clinical experience is still undetermined.]

Carrell [439] enumerates the following as the causes of instability of the foot: a short first metatarsal, a hypermobile first metatarsal segment, metatarsus primus varus and accessory scaphoid or prehallux. He discusses Freiberg's disease and calcaneal apophysitis as well as the use of the Denis-Browne splint.

Lapidus [440] takes issue with the long-held belief that the longitudinal arch of the foot acts as a spring. He shows that the plantar fascia stretches only a small percentage of its length with weight bearing, so that there will be sagging of the apex of the arch of only 0.1 cm. The arch, in his opinion, is a developmental response to the functional requirement for increased strength of the foot as a lever. The integrity of the longitudinal arch is maintained by ligamentous rather than by muscular structures. The muscles of the legs further the support of the longitudinal arch by maintaining a balance between the leg and the foot, by keeping the weight-bearing line in plumb line.

[Ed. Note.—This is an excellent study, and we are in accord with his conclusions.]

Cuttle [441] found that it was difficult to establish the functional ability of a foot by examination and simple physiologic tests. He used the Osgood apparatus for measuring the relative powers of the abductor and adductor groups of muscles. His findings in a study of several hundred recruits corresponded with the clinical observations reported by Osgood. He feels that it may be of assistance in eliminating recruits with disabilities of the foot from the services.

[Ed. Note.—We feel that this is a good approach, but there are other factors that are not considered when only the difference in the strength of muscles is measured.]

Leavitt [442] concludes that the os calcis type of flatfoot may be defined as a postural deformity of the foot in which apparently valgus or eversion of the rear portion of the foot initiates and is responsible for the subsequent deformities associated with depression of the longitudinal arch. Functional deformity of the os calcis type of flatfoot without abnormal congenital protrusion or deformity of the head of the astragalus and especially of the scaphoid can be prevented by subtalar arthrodesis. Symptoms of decompensation or foot strain accompanying this type of flatfoot can most satisfactorily and permanently be corrected by subtalar arthrodesis. It is sometimes necessary to remove the abnormal prominence of the scaphoid.

[Ed. Note.—Flatfoot always starts with valgus at the heel, caused by decompensation. For that reason if the decompensation is eliminated the valgus is corrected. Our feeling, therefore, is that the foot should be fused in the normal position only when the decompensation cannot possibly be corrected by conservative measures, and in our experience this is rare.]

Crisp [443] is of the opinion that the primary cause of valgus strain is fatigue of the tibialis anticus muscle. He talks about contributing factors, however, such as faulty posture, adoles-

439. Carrell, B.: Diagnosis and Treatment of Foot Deformities in Children, Texas State J. Med. **38**:509-511 (Dec.) 1942.

440. Lapidus, P. W.: Misconception About "Springiness" of Longitudinal Arch of Foot: Mechanics of Arch of Foot, Arch. Surg. **46**:410-421 (March) 1943.

441. Cuttle, T. D.: Method for Evaluating Muscle Balance in So-Called "Flat-Foot" in Recruits for the Navy, U. S. Nav. M. Bull. **41**:216-219 (Jan.) 1943.

442. Leavitt, D. G.: Subastragaloid Arthrodesis for Os Calcis Type of Flat Foot, Am. J. Surg. **59**:501-508 (March) 1943.

443. Crisp, E. J.: Mechanics of Valgus Foot Strain, Proc. Roy. Soc. Med. **36**:606-607 (Sept.) 1943.

cence, overweight and in the army heavy boots and long marches. He states that pain results from stretching of the plantar fascia. It is his opinion that the tibialis anticus muscle becomes completely suppressed and the extensor digitorum longus muscle tries to take over the action as a supporter of the longitudinal arch. This results in a clawing of the toes. Therefore there is a muscular incoordination, which he feels it is absolutely essential to rectify. This is done by having a masseuse persuade the patient to relax, train him to dissociate the tibialis anticus muscle from the extensor digitorum longus muscle and teach him to contract the tibialis anticus muscle again.

[ED. NOTE.—We do not agree with the premise that the primary cause of foot strain is fatigue of the tibialis anticus muscle. In our opinion, foot strain is caused by an imbalance between the capacity of the foot to do its work and the load that is placed on the foot. Therefore our therapeutic measures would differ also.]

Billig and Brennan [444] approach the problem of common disorders of the foot by describing a novel type of treatment in 94 cases. They stretched the fascial ligamentous structures of the iliotibial band and of the ligamenta flava. A 1½ inch (3.8 cm.) luggage belt is used to strap the patient firmly to the table, the strap being placed just distal to the anterior superior iliac spines in order to prevent the pelvis from tilting on the spine. The affected leg is adducted and flexed, while the knee is kept extended. They found that this procedure would elicit exacerbation of pain in the foot. They devised some methods and exercises for stretching the ligaments.

[ED. NOTE.—We have recognized a definite relationship between contractures of the ligaments of the thigh and ligaments of the back and mechanical disorders of the foot, and this relationship is on a basis of a functional decompensation, which is present in all these weight-bearing structures. That correction of one will influence another is to be expected.]

Robinow, Johnston and Anderson [445] made a thorough study by means of roentgenograms and accurate measurements of the height of the arches in children from the ages of 4 to 10 years, with and without weight bearing. The conclusion was that most children's arches change but little with age.

Rizzo [446] brings out the importance of women wearing proper shoes when working in industry, and he describes what he considers a good shoe. In addition, he advises exercises for strengthening the feet.

Childress [447] emphasizes that the pathologic changes associated with march fracture are not synonymous with those in march foot. March fracture may occur in bones other than those of the foot. It occurs in the tibia, in the fibula near the proximal or distal end of the bone and in the femur in the distal portion of the shaft and at the neck. Occasionally march fracture may develop in the pelvic bones. He reports a case of march fracture in the cuneiform bone, and this is the first case that has been reported. The lesion is produced by repeated minimal trauma, which by summation causes an overloading of the functional capacity of an otherwise normal bone. The therapy is rest.

Telford [448] describes vascular disturbances, including frostbite, immersion foot, trench foot and shelter foot. Their pathologic features are identical, differing only in the degree of damage. Exposure to cold is the main factor, but prolonged immersion plays an important role. In the majority of cases recovery was good, with no, or at the worst trivial, loss of tissue. In the other cases the patients continued to suffer from symptoms which were due to a combination of sclerosis and deficient blood supply. The after-troubles most often found are pain of a burning or tingling type, increased by warmth or exertion, persistent indurated swelling, chronic and painful ulcers and loss of movement of fingers and toes. Occasionally there is a sensitization to cold. Hyperhidrosis may be troublesome also. These end results are in fact those of a vascular occlusion and resemble closely those found in thromboangiitis obliterans.

In his experience the best method of testing vascular efficiency in the lower extremities is to use a thermocouple thermometer provided with eight or ten leads, each carrying a point for application to the skin. These points are fixed on the areas selected for observation, and a movable plug allows the current from any one point to be recorded by the reflecting galvanometer. The temperatures are recorded, with the patient on the operating table, and at the

444. Billig, H. E., Jr., and Brennan, R. L.: Foot Pains, Mil. Surgeon **92**:539-542 (May) 1943.

445. Robinow, M.; Johnston, M., and Anderson, M.: Feet of Normal Children: Study of Lateral X-Rays of Weight-Bearing Foot, J. Pediat. **23**:141-149 (Aug.) 1943.

446. Rizzo, P. C.: Foot Symptoms: Instruction and Exercises for Their Relief, Indust. Med. **12**:80-81 (Feb.) 1943.

447. Childress, H. M.: March Fractures of the Lower Extremities, War Med. **4**:152-160 (Aug.) 1943.

448. Telford, E. D.: Sympathectomy in Treatment of Cryopathies, Brit. M. J. **2**:360 (Sept. 18) 1943.

end of half an hour's observation of temperature a spinal anesthetic is given and the temperatures again recorded. The normal rise of temperature (14 to 18 degrees F.) in the feet in a young healthy adult is of the order of 8 to 10 degrees C. but in cases such as those under discussion a rise of 1 degree C. (1.8 degree F.) would justify sympathectomy, which can be carried out forthwith.

[ED. NOTE.—For the persistent type of vascular disturbance sympathectomy is of use, but most types respond to conservative measures.]

O'Donoghue [449] has for many years made it a practice at the Crippled Children's Hospital to carry out an operative fusion of the interphalangeal joint of the great toe in all cases of transplantation of the extensor hallucis tendon to the dorsum of the foot. It has been observed that bony fusion of this joint actually occurs in only a comparatively small percentage of these cases. To get bony union he obtained better fixation by careful denudation of the cartilaginous surface of the interphalangeal joint. Then with the toe in satisfactory position a Kirschner wire was drilled linearly through the end of the toe, traversing the distal phalanx, crossing the denuded joint and extending well into the proximal phalanx. This fixation resulted in more frequent bony union.

Goodwin and Swisher [450] discuss the treatment of congenital hyperextension of the fifth toe, with the toe in a markedly adducted position. They advise operation. A Y-shaped incision is made at the base of the involved toe on the dorsum of the foot. The branches of the Y extend diagonally distalward about halfway around the toe. The incision is carried down to expose the extensor tendon. A knife is passed through the tendon, making a horizontal slit about 2 cm. long. The tendon is divided by placing the blade of the knife in the slit and cutting through half of the tendon at the proximal end of the slit and the other half at the distal end of the slit. This is the usual Z-plasty used for lengthening of tendons. The joint capsule is exposed and simply cut at least 180 degrees around the joint. If the original deformity is mainly hyperextension, then the capsulotomy is done mainly on the dorsum. However, if there is severe adduction in the deformity, then the capsulotomy must extend well down on the medial side of the joint. The toe should be freely movable and should assume a normal position without forcing. The toe is placed in this position and maintained there while the severed tendon is repaired; plenty of lengthening is allowed, so that the tendon is loose when the toe is in the normal or slightly flexed position. No repair of the capsule is done.

[ED. NOTE.—In those cases in which there is a tendency for recurrence of adduction, the abductor muscle should be transplanted to retain the position of the toe.]

Hammond [451] describes a procedure for correction of equinus contracture of the great toe. He describes the deformity as being principally due to an elevation of the head of the first metatarsal bone; in other words, there is a dorsal displacement of the head of the first metatarsal bone. Therefore, to correct the flexion of the great toe he brings the first metatarsal bone back to normal position. After the realinement of the first metatarsal bone he fuses it to the cuneiform bone. If there is displacement of the cuneiform also he fuses the cuneiform to the navicular bone. He uses a bone graft extending from the scaphoid to the cuneiform or to the base of the first metatarsal bone. If the flexion deformity is fixed he manipulates the toe to obtain correction.

[ED. NOTE.—This is a rational procedure to correct the deformity. In some cases correction can be obtained by the comma-shaped bar with an inclined plane, which brings the head of the metatarsal bone down to the correct position. If the contracture is so severe that it cannot be corrected conservatively, then osteotomy may be necessary to correct the deformity.]

Pruce and Hagen [452] describe 8 cases of clawing of the great toe resulting, in their opinion, from improper application of a plaster cast. They have also seen the condition following poliomyelitis and with Friedreich's ataxia. They stress the importance of prevention of the condition, emphasizing that a cast should always go up under the tips of the toes and be molded well to retain the normal arches. The occurrence of this deformity delays recovery.

[ED. NOTE.—In view of this article, it may still be necessary to emphasize that a cast should always go up to the tips of the toes on the plantar surface.]

449. O'Donoghue, D. H., and Stauffer, R.: Improved Operative Method for Obtaining Bony Fusion of Great Toe, Surg., Gynec. & Obst. **76**:498-500 (April) 1943.

450. Goodwin, F. C., and Swisher, F. M.: The Treatment of Congenital Hyperextension of Fifth Toe, J. Bone & Joint Surg. **25**:193-196 (Jan.) 1943.

451. Hammond, G.: Elevation of First Metatarsal Bone with Hallus Equinus, Surgery **13**:240-256 (Feb.) 1943.

452. Pruce, A. M., and Hagen, W. H.: Clawing of Great Toe Following Improper Application of Plaster, J. A. M. A. **123**:955-956 (Dec. 11) 1943.

Mair [453] reports an unusual case of plantar dislocation of the head of the fourth metatarsal bone. The mechanism of injury is not understood. It was treated by operative reduction.

A suggestion is presented by Jergesen [454] to prevent the concomitant occurrence of a valgus deformity of the normal foot during treatment of unilateral congenital talipes equinovarus with the Thomson modification of the Denis-Browne splint. He flexes the uninvolved hip to about 90 degrees and then adjusts the plate. After the adjustment he observes that the normal foot assumes the position of slight inversion, regardless of the position the leg may assume.

[ED. NOTE.—This is a recommendation for those who use the Denis-Browne splint.]

Morris [455] has treated with skeletal traction 52 recurrent clubfeet, 3 acquired clubfeet and 6 cavus feet. All the patients were children between the ages of 2 to 12 years. He recommends skeletal traction as a method that is relatively atraumatic and quick. He runs Kirschner wires through the tibia, the os calcis and the necks of the metatarsal bones. The wire through the tibia is inserted at the junction of about the upper and middle thirds of the tibia. Distraction is applied along the axis of the foot and maintained with a metal apparatus. Rods connect the Kirschner wires. The apparatus is illustrated, showing threaded distracting rods. He was able to obtain good corrections but was not able to retain them. His results showed failure to maintain correction in 40 per cent of the feet treated, which was due to deformity of the tarsal bones by too vigorous previous treatment. He does not believe that skeletal traction itself is a cure for deformities of the foot but believes that it can overcorrect the contractures. The maintenance of correction depends on completeness of the overcorrection as well as holding the foot in the overcorrected position for a sufficient length of time.

[ED. NOTE.—In our opinion, better results should be obtained by the usual conservative measures, so that there is not such a high percentage of recurrences. Even after recurrence, manipulative correction has given much better results in our hands than this type of treatment. For severe deformities we use the Haglund board abetted by the Thomas wrench to correct the heel.]

Bohnsack and Andes [456] report the results of treatment in 302 cases of sprained ankle. In some cases they strapped the ankle and permitted early use, and in other cases they sprayed it with ethyl chloride and permitted early use. The ankles which were strapped were soaked in ice-cold water for thirty minutes before strapping if they were seen immediately. They feel that instead of using ethyl chloride it would be just as well, if not better, to use local injection of procaine hydrochloride.

Pennal [457] describes simple sprains and recommends injection of procaine hydrochloride, then adequate strapping and early functional activity. If the sprain is severe with rupture of the anterior and middle bands of the external lateral ligament, a momentary subluxation of the astragalus should be suspected. Aids in diagnosis are evidence of tilting of the astragalus and roentgenograms taken with the heel in extreme varus. The treatment requires prolonged immobilization by means of a walking cast, in most cases for about ten weeks. In cases of recurrent subluxation the diagnosis is made by rocking the astragalus and confirmed by roentgenograms taken with the foot held in inversion. In his series of cases Pennal used an outside crooked and elongated heel or an inside iron and T strap. The other alternative was an operative reconstruction of the external lateral ligament. He prefers the Watson-Jones technic.

Roberts [458] draws attention to the fact that in cases of sprained ankle the astragalus is sometimes tilted, as seen in roentgenograms taken with the heel fully inverted. In these cases recovery is slow and unsatisfactory, so that the sprain is sometimes worse than a fracture. He describes the ligaments which may be torn in the sprain, either the internal or the external lateral ligament, and he tells how to protect the ligament by means of zinc oxide or adhesive tape strapping. For chronic sprains in which there are a weak ligament and recurring displacement he advises an operation, usually one in which an external lateral ligament is made from the peroneus brevis tendon. With regard

453. Mair, G. B.: Plantar Dislocation of Fourth Metatarsal, Brit. M. J. **2**:169 (Aug. 7) 1943.

454. Jergesen, F. H.: Treatment of Unilateral Congenital Talipes Equinovarus with Denis-Browne Splint, J. Bone & Joint Surg. **25**:185-187 (Jan.) 1943.

455. Morris, R. H.: Skeletal Traction as Method of Treatment for Certain Foot Deformities, Arch. Surg. **46**:736-742 (May) 1943.

456. Bohnsack, R. W., and Andes, J. E.: Ankle Sprains: Incidence, Treatment, Diagnosis and Lost Time Incurred, Indust. Med. **12**:588 (Sept.) 1943.

457. Pennal, G. F.: Subluxation of Ankle, Canad. M. A. J. **49**:92-95 (Aug.) 1943.

458. Roberts, N.: Treatment of Minor Injuries of Ankle, Post-Grad. M. J. **19**:7-11 (Jan.) 1943.

to the injection of procaine hydrochloride in the treatment of sprains, he feels that there is remote danger of sepsis and also danger that the true nature of the injury may not be recognized. He feels that the chief values of procaine is its capacity to make the injured point painless, so that one can have a free hand to test clinically and roentgenographically for any potential instability.

Leinwand [459] describes a method of injection of procaine hydrochloride for the treatment of sprains, and as contraindications he names open wounds, infection or potential infection in the injured area, rupture of a large or medium-sized vessel and idiosyncrasy to the drug. He advocates the procedure for general use in military practice, particularly in the field or in landing forces, where the materials necessary may be incorporated in a field medical kit. He believes that it is a safe and convenient aid to maintain a policy of keeping as many men at as many guns as many days as possible.

McMaster [460] believes that recovery from sprain of the ankle is greatly hastened by active and continued use of the joint, regardless of what other local treatment is adopted. Injection of procaine hydrochloride makes possible early motion and elimination of pain. Over 90 per cent of sprains of the ankle involve the anterior talofibular ligament. Roentgenograms should be taken before treatment is started, to exclude fractures.

Bakst and McCormick [461] use local anesthesia for sprains of the ankle and also recommend it for injuries of the chest and back. Immediate and complete relief of pain makes it possible for the patient to get back to work sooner and also reduces the necessity for sedatives and narcotics. He recognizes the fact that it cannot be used for open wounds.

Smart [462] emphasizes the importance of maintaining the physiologic activity of muscles at its maximum in the treatment of strained muscles and sprained joints, particularly in the early stages. He discusses the complication of injury to soft structures and advises graduated painless contractions produced by electrical stimulation immediately after the injury, which will result in beneficial physicochemical changes. In the later stages of injury, when muscles have become atonic and wasted, a point may be reached at which only limited muscular contraction can be initiated voluntarily. In such cases the beneficial effect of graduated contractions produced by electrical stimulation has only to be seen in order to bring full realization of the inestimable value of this method of treatment of muscles.

Outland [463] states that injuries to the anterior inferior tibiofibular ligament without serious fractures are frequent. If subluxation accompanies a sprain, disability always follows. In the early treatment he uses an unpadded walking cast. For a chronic condition he suggests the use of a bone graft taken from the tibia of the same side. Then a hole is driven through the tibia and fibula and the bone graft inserted.

Burns [464] brings out the fact that there is a good deal of trouble in the treatment of the abduction fracture of the ankle, and he feels that it is due to rupture of the tibial fibular ligament and diastasis. To correct this diastasis he first used a bolt driven through the tibia and fibula above the ankle. He now uses wire inserted through two parallel drill holes.

[Ed. Note.—Our feeling is that the injection of procaine hydrochloride is of value, particularly in those cases in which it is certain that the injury is minor, in other words, a tear of the ligament that can heal in normal position with weight bearing. It is particularly useful inasmuch as it relieves pain and muscular spasm. In some instances muscular spasm persists, owing to irritation of the injured ligament, and holds the foot in valgus. With injection of procaine hydrochloride in these cases the foot can go back to normal position, and spontaneous recovery will occur. The dangers of the injection method, as has been pointed out in the articles reviewed, are in addition to the contraindications the fact that it masks the real lesion and may permit the occurrence of a serious deformity. In cases of severe ligamentous tear there frequently is tearing of the tibiofibular ligament. If this ligament is torn and not protected by accurate fixation, diastasis occurs, which becomes

459. Leinwand, I.: The Use of Local Anaesthesia in the Treatment of Sprains (or Local Tissue Injury Without Open Wounds), Mil. Surgeon **92**:60-62 (Jan.) 1943.

460. McMaster, P. E.: Treatment of Ankle Sprain: Observations in More Than Five Hundred Cases, J. A. M. A. **122**:659-660 (July 3) 1943.

461. Bakst, H. J., and McCormick, G. W.: Use of Local Anesthesia in Treatment of Contusions and Sprains, U. S. Nav. M. Bull. **41**:107-111 (Jan.) 1943.

462. Smart, M.: Early Treatment of Strains and Sprains by Graduated Muscular Contractions, Brit. J. Phys. Med. **6**:76-81 (May-June) 1943.

463. Outland, T.: Sprains and Separations of the Inferior Tibiofibular Joint Without Important Fracture, Am. J. Surg. **59**:320-329 (Feb.) 1943.

464. Burns, B. H.: Diastasis Fracture of Inferior Tibiofibular Joint, Proc. Roy. Soc. Med. **36**:330-332 (May) 1943.

permanent and causes disability. The early recognition of this lesion and proper treatment prevent future trouble. Our chief use of the injection, aside from eliminating muscular spasm, is to aid in diagnosis. With the injection method for the painful sprain, the foot can be brought into extreme inversion or eversion and instabilities can be detected that would not ordinarily show in the routine roentgenograms.]

McElvenny [465] states that Morton's toe is often resistant to conservative treatment. It is caused by a tumor involving the most lateral branch of the medial plantar nerve. Careful palpation will usually reveal the tumor, which lies high in the web between the third and fourth toes. If symptoms justify it, excision of the tumor should be done. The author reports on 11 patients treated by operation. Of the 12 tumors removed from 11 patients, 5 had been studied microscopically and appeared to be either neurofibromas or angioneurofibromas. Grossly they were fatty and soft on the outside and firm, white and fibrous toward the center. The plantar nerve was embedded in the center.

Hauser [466] reports a case of neurofibroma in the deep plantar nerve, which is a rare tumor. At the time of resection he emphasizes that sufficient nerve be removed so that the section is done through normal nerve tissue, to lessen the chances of recurrence. The term "neurinoma" avoids the implications as to the origin of the tumor cells suggested by "neurofibroma" or schwannoma. The tumor showed cells having large, vesicular, elongated nuclei of oval or spindle shape. These were arranged in large concentric whorls with rather abundant mucoid intercellular substance. The cells were rather uniform in appearance throughout the section. In some regions small concentric whorls were seen, but for the most part the tumor cells were rather loosely arranged, showing a slight tendency toward palisading of the nuclei. There were no areas of increased density, increase in mitotic figures or invasion of the capsule to indicate that the tumor might be malignant.

Gaston [467] describes in detail a bone block for paralytic drop foot, which incorporates removal of the distal attachment of the achilles tendon with an attached piece of bone. Care is taken to avoid disturbing tissue lying posterior to the ankle joint and at the lower end of the tibia, so as to avoid postoperative proliferation of bone.

[Ed. Note.—We feel that the bone block that goes under the tibia instead of posterior to it is more satisfactory. The procedure is equally simple and more durable.]

Greene [468] describes a refrigerator that was developed in collaboration with R. J. Simpson of the International Refrigerator Company. They designed an apparatus in which the extremity can be put through an opening in a cabinet in a compartment in which the temperature can be controlled.

[Ed. Note.—He has had no opportunity for clinical application, but it makes sense to us that an apparatus which will control temperatures might be of some aid when it is necessary to obtain lesser degrees of cold.]

Causton [469] describes a technic for taking a roentgenogram of the sesamoid bones in the region of the first metatarsophalangeal joint. With the patient lying in a prone position the great toe rests in a position of hyperextension; the film is supported under the first metatarsophalangeal joint and the tube adjusted so that the central ray, which is vertical, passes between the sesamoid bones. A further view is obtained with the patient on his uninjured side. The film is placed under the distal portion of the first metatarsal bone and is allowed to conform to the natural slope of the medial aspect of the foot. The tube is then adjusted so that the central ray passes through the medial sesamoid bone and makes an angle of 40 degrees with the film.

Gottlieb [470] believes that a definite clinical entity is brought about by a diseased sesamoid bone. He describes 11 cases, in 10 of which the patients were women who all wore high-arched shoes, with excessive weight on the first joint. The symptoms were usually unilateral. He does not believe that the bone was fractured. The cause of the disease is repeated trauma. He recommends conservative treatment first, which consists of resting, immobilization and relief of weight bearing on the affected area, the injection of procaine hydrochloride and other physical therapeutic measures. Only when these have failed should removal of the affected bone be carried out.

465. McElvenny, R. T.: The Etiology and Surgical Treatment of Intractable Pain About the Fourth Metatarsophalangeal Joint (Morton's Toe), J. Bone & Joint Surg. **25**:675-679 (July) 1943.

466. Hauser, E. D. W.: Neurofibroma (Neurinoma) of Foot, J. A. M. A. **121**:1217-1219 (April 10) 1943.

467. Gaston, J. H.: Modified Bone Block for Paralytic Foot Drop, South. M. J. **36**:336-338 (May) 1943.

468. Greene, R.: Cold in Treatment of Damage Due to Cold, Lancet **2**:695-697 (Dec. 12) 1942.

469. Causton, J.: Projection of Sesamoid Bones in Region of First Metatarso-Phalangeal Joint, Radiotherapy **9**:39 (May) 1943.

470. Gottlieb, A.: Diseased Tibial Sesamoid of Big Toe Joint, West. J. Surg. **51**:193-195 (May) 1943.

Cane [471] reports a case of neglected congenital equinovarus, in which treatment included removal of the talus in addition to lengthening of a tendon.

[ED. NOTE.—This method did improve the situation in the case which he reports.]

Smith [472] uses the Keller-Brandes type of operation for hallux valgus. The technic consists in a partial phalangectomy of the proximal portion of the first phalanx of the great toe. It is a relatively simple procedure and allows early return to function. It does give good results in hallux rigidus.

[ED. NOTE.—We feel that this is a good procedure for hallux rigidus, but on hallux valgus and the concomitant deformity it has little influence.]

Lewis [473] reports 8 cases of the less common lesions of the astragalus, to call attention to the wide variety of pathologic changes occurring in this bone. His report includes the following types of disease: tuberculosis, staphylococcic osteomyelitis, osteochondritis dissecans, aseptic necrosis, osteochondroma, osteitis fibrosa cystica, chondromatous giant cell tumor and metastatic adenocarcinoma.

Cobey [474] reports 3 cases of osteochondritis of the dorsal articular surface of the astragalus. He recommends roentgen examination for severe sprains, keeping in mind the possibility of this rare condition. The presence of a loose body in this joint leads to arthritic changes, and early removal of the loose fragment is recommended.

Lipscomb and Ghormley [475] say where possible fractures of the astragalus should be reduced by closed manipulative procedures, followed by fixation by means of a plaster of paris cast. No weight bearing should be allowed for eight to ten weeks. When it is not possible to get a good reduction by manipulative measures they recommend an open operation. They use a lateral incision along the ankle at the level of the subastragaloid joint. The peroneal tendon can be displaced or if necessary divided and repaired later. After reduction of the fracture the position can be held by means of screws. They prefer vitallium screws. When the damage is severe and the displacement great, astragalectomy is done. In old cases in which there is a great deal of pain arthrodesis is sometimes necessary. He feels that the pain is often due not to the failure of union but to the arthritic changes that occur.

McLaughlin [476] states that in the majority of the reported cases rupture of the achilles tendon is due to strenuous physical exercises. For treatment he advises operative repair. The tendon usually tears at the junction of the tendon and the muscular portion of the gastrocnemius muscle. He uses silk sutures for repair and maintains fixation in the original cast for about six weeks and then brings the foot to a right angle to the leg two weeks following surgical operation, with return to full activity in from nine to twelve weeks.

[ED. NOTE.—In our experience rupture of the achilles tendon is not such an infrequent occurrence, but many of them are partial tears that can be treated effectively by conservative measures. The severe ones should be repaired.]

Paulson [477] encountered a severe injury of the navicular bone of the foot, which was giving symptoms. He removed the navicular bone entirely and obtained a good functional result.

O'Donoghue and Sell [478] report a case of congenital talonavicular synostosis. It is a rare condition, which was described originally in 1879 by Anderson, who reported a bilateral condition. In the case reported here the synostosis was bilaterally symmetric.

Daseler and Anson [479] give a report on the plantaris muscle, based on a review and a study of 750 consecutive specimens. They regard the plantaris muscle and tendon as the vestigial remains of a primitive flexor muscle of the toes, which, originally continuous with the plantar aponeurosis, later was rendered discontinuous through intermediate attachment to the calcaneum. The plantaris muscle and its tendon are subject to considerable variation in both

471. Cane, L. H.: Congenital Talipes Equinovarus Corrected by Talectomy, East African M. J. **20**:2-4 (Jan.) 1943.

472. Smith, P. E.: Hallux Valgus: Consideration of Keller-Brandes Operation, Mississippi Doctor **20**:445-450 (March) 1943.

473. Lewis, R. W.: Less Common Lesions of the Astragalus, Ann. Surg. **116**:891-897 (Dec.) 1942.

474. Cobey, M. C.: Osteochondritis Dissecans of the Astragalus, Mil. Surgeon **93**:184-186 (Aug.) 1943.

475. Lipscomb, P. R., and Ghormley, R. K.: Old and New Fracture-Dislocations of the Astragalus, S. Clin. North America **23**:995-1011 (Aug.) 1943.

476. McLaughlin, C. W., Jr.: Complete Rupture of Tendo-Achilles: Report of Case, U. S. Nav. M. Bull. **41**:1388-1391 (Sept.) 1943.

477. Paulson, E. C.: Foot Functions Following Loss of the Tarsal Navicular, Minnesota Med. **26**:545-547 (June) 1943.

478. O'Donoghue, D. H., and Sell, L. S.: Congenital Talonavicular Synostosis: A Case Report of a Rare Anomaly, J. Bone & Joint Surg. **25**:925-927 (Oct.) 1943.

479. Daseler, E. H., and Anson, B. J.: Plantaris Muscle: Anatomical Study of 750 Specimens, J. Bone & Joint Surg. **25**:822-827 (Oct.) 1943.

the point of origin and the point of insertion. In an examination of 150 lower extremities, the authors have encountered four types of insertion of the tendon. Of 750 consecutive lower extremities examined by the authors the plantaris muscle was absent in 50 (6.67 per cent). In one third of the specimens in which the muscle was missing, the absence was bilateral. The surgical utilization of the plantaris tendon is particularly indicated as a desirable substitute for the fascia lata in hernial repair, transplantation of tendons and repair of ligaments.

[ED. NOTE.—Another significance of the plantar muscle is that in lengthening the achilles tendon it must be divided because it is a separate muscle.]

Albert and Mitchell [480] report 3 cases of Volkmann's ischemia of the leg. They recommend early recognition of the condition and early surgical intervention. The harmful results of a skin-tight plaster cast are stressed.

480. Albert, M., and Mitchell, W. R. D.: Volkmann's Ischemia of Leg, Lancet **1**:519-522 (April 24) 1943.

XIII. TUBERCULOSIS OF BONES AND JOINTS

PREPARED BY ALAN DE FOREST SMITH, M.D., NEW YORK

In a study by Tytler and Lapp,[481] promin (sodium salt of p,p'-diamino-diphenylsulfone-N-N'-didextrose sulfonate) in a concentration of 5 per cent in a medium of tragacanth jelly was repeatedly injected, after aspiration of pus, into tuberculous abscesses and sinus tracts of 10 patients. The abscesses treated were in the following regions: 4 in the lumbar region, 2 in the groin, 1 in the low dorsal region, 1 in the axillary region, 1 in the right ilium and 1 in the neck. While the results were somewhat irregular, the clinical opinion was formed that improvement in all patients was greater or more rapid than would have been expected with orthodox methods. It is thought that these results justify a more extensive trial of the drug by local application to suitable lesions and possibly by injection into more deep-seated lesions.

Callomon [482] found that experimental tuberculosis of guinea pigs was apparently somewhat inhibited by administration of promin, 4 (alpha-pyridil-N-sulfonamido)-phenyl-2-azo-8-amino-1-naphthol-5, 7 disulfonic acid and disodium formaldehyde sulfoxylate diaminodiphenylsulfone. Results with the first and third of these compounds were considered as encouraging for further investigation. Sulfanilamide, sulfapyridine, sulfathiazole and sulfathiazolline showed no appreciable effect under the same conditions of experimentation.

Feldman and Hinshaw [483] studied the tuberculotherapeutic efficiency of two compounds of the sulfonamide series and four of the sulfone series in guinea pigs which six weeks previously had been inoculated subcutaneously with human tubercle bacilli. Drugs were administered for one hundred and twenty-eight days, after which time all the control animals were dead, and the experiment was terminated. The lowest mortality rate, 19 per cent, was in the promin-treated group; that in the group treated with sulfadiazine and another sulfonamide compound was 71 per cent. The results indicated definitely the superiority of the derivatives of 4, 4'-diaminodiphenylsulfone over compounds containing a sulfonamide nucleus.

Steinbach and Duca [484] found promin in vitro to be bacteriostatic for every acid-fast bacillus tested, including saprophytes and piscine, avian, human and bovine tubercle bacilli. Promin given to guinea pigs subcutaneously three times daily starting with the day of experimental infection exerted a retarding effect on the course of the tuberculosis. Although promin influences the disease in the experimental animal to a greater extent than any other chemotherapeutic agent which the authors have tested, it is extremely toxic. Results were promising in 6 of 11 cases of advanced human pulmonary tuberculosis in which promin was administered, but a large series of cases will be required before conclusions can be drawn as to the efficacy of the drug in man.

McClintock and Goodale [485] report that in vitro a 12 mg. per hundred cubic centimeter solution of the potassium salt of the sulfapyridine-choleate complex appears to inactivate tubercle

481. Tytler, W. H., and Lapp, A. D.: Treatment of Superficial Tuberculous Lesions by Local Application of Promin, Brit. M. J. **2**:748-749 (Dec. 26) 1942.

482. Callomon, F. F. T.: New Derivatives of Diaminodiphenylsulfone: Their Therapeutic Effect in Experimental Tuberculosis of Guinea Pigs, Am. Rev. Tuberc. **47**:97-106 (Jan.) 1943.

483. Feldman, W. H., and Hinshaw, H. C.: Comparative Effects of Six Compounds Administered with Therapeutic Intent to Tuberculous Guinea Pigs, Am. J. Clin. Path. **13**:144-147 (March) 1943.

484. Steinbach, M. M., and Duca, C. J.: Chemotherapy in Tuberculosis, Tuberculology **6**:93-95 (May) 1943.

485. McClintock, L. A., and Goodale, R. H.: Use of Choleate Principle in Treatment of Tuberculosis, U. S. Nav. M. Bull. **41**:708-713 (May) 1943.

bacilli after eight days' incubation. The ability of the drug to inhibit the growth of tubercle bacilli in vivo has been borne out by experiments on animals. Of 160 treated animals (guinea pigs), 31 died as a result of combined action of the drug and coccidiosis. Of the remaining 129 animals, 2 showed tuberculosis grossly and microscopically. All of the others gave negative reactions. Most of the control animals died within fifty days of extensive tuberculosis. It is felt that the complex exerts an inhibitory effect on the tubercle bacillus in vitro and in vivo.

Medlar and Sasano [486] administered promin to guinea pigs for five months, beginning ten days after virulent tubercle bacilli had been injected subcutaneously. The last survivor was killed eighteen months after therapy was stopped. Ninety-two per cent of the animals in the promin-treated group, in contrast with 36 per cent in the untreated control group, were alive when therapy was discontinued. In the promin-treated group 24 per cent died of uncomplicated generalized tuberculosis; 28 per cent exhibited small localized tuberculous foci in the spleen, liver or lungs, and 48 per cent showed no macroscopic evidence of visceral tuberculosis, though in 77 per cent of these cultures tubercle bacilli were obtained from the spleen. Promin, therefore, retarded decidedly but did not eradicate the tuberculous infection. Results to be expected from any chemotherapeutic method for tuberculosis must be tempered by knowledge that the disease is chronic, that the repair of damage to tissue is slow and that the majority of tuberculous patients in sanatoriums have only a limited resistance to the infection. The extermination of the infecting agent with promin therapy should not be anticipated, but these favorable experimental results warrant further chemotherapeutic studies to reveal compounds that may be even better than promin.

[Ed Note.—These experiments give some promise that the effort to discover a drug which will have an influence on the tubercle bacillus comparable to that of the sulfonamide compounds on many of the pyogenic organisms may be successful. Thus far the therapeutic value of promin seems far from being established, however.]

Perlman and Freiberg [487] describe 5 cases of tuberculosis of the lumbar portion of the spine in adults in which there was an osseous bridge between two of the bodies. In 4 this was complete and in the fifth partial. The diagnosis was proved in 4 cases by demonstration of tubercle bacilli or by positive results of guinea pig inoculation with the pus from an abscess. In the fifth case the diagnosis was presumptive from the finding of tubercle bacilli in multiple cutaneous lesions.

[Ed. Note.—These findings are of importance chiefly from the standpoint of diagnosis. The bridging of the bodies which took place in these cases probably was not extensive enough to be relied on for fixation. It has been pointed out that a mild type of osteomyelitis frequently involves the spine and that one of the characteristics which differentiates such a pyogenic infection of the vertebrae from tuberculosis is early bony union of the bodies. This condition practically always follows a pyogenic infection elsewhere and is associated with a greater degree of pain. The differential diagnosis between tuberculosis and a pyogenic infection in a lesion associated with bridging of the bodies might be difficult in some cases but usually can be made with a reasonable degree of certainty by laboratory tests and on the basis of the existence of associated lesions. It is important to differentiate the two, because fusion is indicated for tuberculosis and not only is futile for pyogenic osteomyelitis but may be detrimental.]

486. Medlar, E. M., and Sasano, K. T.: Promin in Experimental Tuberculosis in Guinea Pig, Am. Rev. Tuberc. **47**:618-624 (June) 1943.

487. Perlman, R., and Freiberg, J. A.: The Bridging of the Vertebral Bodies in Tuberculosis of the Spine, J. Bone & Joint Surg. **25**:340-350 (April) 1943.

XIV. CHRONIC ARTHRITIS

PREPARED BY LORING T. SWAIM, M.D., BOSTON

General Considerations.—Because of the war there have been fewer articles and possibly less original research work on arthritis reported in 1943 than in previous years. Nevertheless there are certain articles of interest. Burbank [488] gives an interesting review of arthritis through the ages, stating that evidence of arthritis was present in the fossilized remains at the beginning of the reptilian age, when vertebrates started to inhabit the globe; the first skeletal proof of arthritic changes was found to date back to this period. He also draws attention to the fact that many of the great men of history had

488. Burbank, R.: Arthritis Through the Ages, Tri-State M. J. **15**:2903-2911 (March) 1943.

arthritis; among them were Julius Caesar, Alexander Farnese, Frederick the Great and others.

Seltzer,[489] a research fellow in physical anthropology at Harvard, reports on a series of almost 400 patients from the Robert Breck Brigham Hospital after careful anthropometric measurements. He decides that patients with rheumatoid arthritis are remarkably different in bodily physique from those with degenerative disease of the joints.

> The physical differences between the two groups were often of such magnitude that the level of statistical significance was reached in the case of a very large number of measures. This occurred in spite of the small size of the series involved. . . . From the profusion of detailed differentiae the degenerative joint disease group may be roughly described as being bigger, heavier, and more lateral in body build than the rheumatoid arthritics. . . . Although it is true that the rheumatoid arthritics are more linear in body build than the degenerative joint disease group, the results of this investigation do not agree with the impressions of many clinicians who stress the linearity and distinctiveness of the rheumatoids. . . . The degenerative joint disease group exhibits greater anthropological distinctiveness and homogeneity than the rheumatoids.

He believes that the physical characteristics of patients with degenerative arthritis have some bearing on the type of arthritis. He finds the same true for men and for women.

Of general interest also is the study of Stone [490] in which 22 cases of rheumatoid arthritis were studied from a neurologic and an endocrinologic aspect. He found that with vitamin E (wheat germ oil) and fever therapy improvement occurred in 17 of 22 cases.

Pain is a problem of great significance, according to Smyth and Freyberg,[491] and needs control by rest, splints, drugs, roentgen treatment and physical means.

Treusch and Krusen [492] found, in a study of 218 patients with all types of arthritis for whom home physical therapy was recommended, that 92.7 per cent of the patients carried out the treatment. The number of patients who continued treatment depended on the number of individual lessons given. [ED. NOTE.—This is of interest from the point of view of a planned schedule.]

Banghart [493] believes that he can control pain by the use of bee venom, but he finds only one preparation of real value: apis mellifica, which is distributed by John A. Borneman and Sons. Of 16 cases he found the improvement marked in 9, moderate in 5 and poor in 2. In 4 of the 16 cases a second course of injections was required. There were no good results in the 4 cases of Marie-Strümpell disease. As with many forms of treatment, the results seem to depend on the type of material used.

Hartung [494] believes:

> A simultaneously applied program of constitutional rehabilitation, gold salts, whole blood transfusions, and prevention and treatment of deformities will produce satisfactory results in over half of the patients with rheumatoid arthritis.

Ludwig, Short and Bauer [495] observed an increase of protein in the cerebrospinal fluid in 101 arthritic patients. Forty-two had spondylitis, and 59 had peripheral arthritis. Fifteen of the 16 patients with increased protein in the cerebrospinal fluid had either spondylitis or symptoms suggesting spinal involvement. Apparently the increased protein content depended on inflammatory activity about the spine.

> Attention is called to the diagnostic difficulties presented by patients with rheumatoid spondylitis and increased cerebrospinal-fluid protein, with particular reference to their differentiation from cases with ruptured intervertebral disks.

Fingerman and Andrus [496] found lesions of rheumatic heart in 31 per cent (or 19) of 61 autopsies. In 6 of the 19 there was evidence of congestive heart failure, with chronic passive congestion of the liver; amyloidosis of one or several organs was observed in 13 and glomerulitis in 8. These findings agree with those of Bayles and others who have reported the prevalence of cardiac conditions with rheumatoid arthritis.

489. Seltzer, C. C.: Anthropometry and Arthritis: Differences Between Rheumatoid and Degenerative Joint Diseases; Females, Medicine **22**:189-203 (May) 1943; Anthropometry and Arthritis: Differences Between Rheumatoid and Degenerative Joint Disease; Males, ibid. **22**:163-188 (May) 1943.

490. Stone, S.: Neurological and Endocrine Aspects of Atrophic Arthritis (Deformans): Report on Use of Vitamin E and Artificial Fever, J. Nerv. & Ment. Dis. **97**:638-655 (June) 1943.

491. Smyth, C. J., and Freyberg, R.: Significance and Management of Joint Pain, J. Michigan M. Soc. **42**: 818-822 (Oct.) 1943.

492. Treusch, J. V., and Krusen, F. H.: Physical Therapy Applied at Home for Arthritis: Follow-Up Study with Supplementary Summary of Sedimentation Rate of Erythrocytes in 229 Cases of Arthritis, Arch. Int. Med. **72**:231-238 (Aug.) 1943.

493. Banghart, H. E.: Bee Venom for Relief of Arthritic and Rheumatic Pain, Hahneman. Monthly **78**: 19-22 (Jan.) 1943.

494. Hartung, E. F.: Treatment of Rheumatoid Arthritis Including Gold Salts Therapy, Bull. New York Acad. Med. **19**:693-703 (Oct.) 1943.

495. Ludwig, A. O.; Short, C. L., and Bauer, W.: Rheumatoid Arthritis as Cause of Increased Cerebrospinal Fluid Protein: Study of 101 Patients, New England J. Med. **228**:306-310 (March 11) 1943.

496. Fingerman, D. L., and Andrus, F. C.: Visceral Lesions Associated with Rheumatoid Arthritis, Ann. Rheumat. Dis. **3**:168-181 (May) 1943.

Fraser [497] reports 61 cases of rheumatoid arthritis in which he tried to follow Cecil's technic for making blood cultures. He recovered no streptococci. He did recover diphtheroid bacilli in 3 cases. He draws attention to the fact that bacteremia due to trauma or treatment such as massage may occur and cause a blood culture to elicit a positive reaction.

[Ed. Note.—In the Manual of Occupational Therapy [498] an excellent article has been written on occupational therapy for arthritis. It is well worth studying. It takes up the various main points: (1) rest through diversion; (2) constructive exercises; (3) prevention of neurosis and helplessness, and (4) importance of emotional outlet and readjustment for the future. The occupation should provide exercise for the joints and muscles.

Another primer has been written by the Committee of the American Rheumatism Association and has been published in *The Journal of the American Medical Association.*[499] This is an excellent review of the present knowledge of arthritis. It can be secured from *The Journal of the American Medical Association.* It carries the names of authorities in the United States.]

Bauer and Engleman [500] draw attention to a syndrome of unknown cause which is characterized by urethritis, conjunctivitis and arthritis. It is called Reiter's disease. They hope that clinicians and bacteriologists will watch for this syndrome.

From a nutritional angle, Bayles, Richardson and Hall [501] report 31 cases in which the prerheumatic diet was studied. They come to the conclusion that it is not different from the usual American diet and that if a food factor contributes to the onset of rheumatoid arthritis their studies suggest that it may be caused by the increased total requirement of the patient rather than a deficiency diet. They feel that because of the frequent deficiency states found the disease itself may increase the requirements of food, especially of the vitamin B complex.

Gout.—This disease is still being found and studied. Bartels,[502] of the Lahey Clinic, reports treatment with a diet low in purine and fat and high in carbohydrate and cinchophen.

On this plan of treatment seven minor attacks of gout occurred, as compared with 84 major attacks during a comparative period before treatment. This plan of treatment secured the desired results of reducing the blood uric acid level and reducing the number and severity of further attacks of gout. Even patients in the phase of chronic gouty arthritis responded to this plan of treatment.

They believe that cinchophen is not so dangerous when given with carbohydrate and protein.

Linton and Talbott [503] report the excellent results of removal of tophaceous deposits in 11 patients, with relief of pain and restoration of function. They describe the operative procedures and point out the necessity of good medical care. They stress the resultant "improved cosmetic appearance and in many instances permanent eradication of tophaceous deposits" and "adequate preoperative and postoperative treatment of the patient with colchicine."

Neuwirth [504] writes to the contrary. He emphasizes the dangers and later effects of using cinchophen. He points out that the cause of hyperuricemia, of retention of urates and of precipitation of sodium urate is not yet known.

Research still goes on, however. Oppenheimer and Kunkel,[505] in the *Bulletin of the Johns Hopkins Hospital,* report on the injection of a solution of the enzyme uricase, extracted from pig's liver. This was given intramuscularly after being made bacteria free by filtration. The extract remains active about two months when frozen and stored at — 28 C.

Single injections of this purified uricase extract can produce a sharp lowering of the plasma uric acid of "gouty" chickens. . . . Continued daily administra-

497. Fraser, T. N.: Blood Cultures in Rheumatoid Arthritis: Historical and Personal Observations, Ann. Rheumat. Dis. **3**:181-190 (May) 1943.

498. Occupational Therapy: Manual Prepared by Council of Physical Therapy of American Medical Association, Committee of American Occupational Therapy Association and Subcommittee on Physical Therapy and Committee on Information of Division of Medical Sciences of National Research Council, War Med. **3**: 635-656 (June) 1943.

499. Jordan, E. P., and others: Primer on Arthritis Prepared by Committee of American Rheumatism Association, Rev. Asoc. méd. argent. **56**:532-542 (Sept. 15-30) 1942; J. A. M. A. **119**:1089-1104 (Aug. 1) 1942.

500. Bauer, W., and Engleman, E. P.: Syndrome of Unknown Etiology Characterized by Urethritis, Conjunctivitis, and Arthritis (So-Called Reiter's Disease), Tr. A. Am. Physicians **57**:307-313, 1942.

501. Bayles, T. B.; Richardson, H., and Hall, F. C.: Nutritional Background of Patients with Rheumatoid Arthritis, New England J. Med. **229**:319-324 (Aug. 19) 1943.

502. Bartels, E. C.: Successful Treatment of Gout, Ann. Int. Med. **18**:21-28 (Jan.) 1943.

503. Linton, R. R., and Talbott, J. H.: Surgical Treatment of Tophaceous Gout, Ann. Surg. **117**:161-182 (Feb.) 1943.

504. Neuwirth, E.: Milestones in Diagnosis and Treatment of Gout, Arch. Int. Med. **72**:377-387 (Sept.) 1943.

505. Oppenheimer, E. H., and Kunkel, H. G.: Further Observations on Lowering of Blood Uric Acid by Uricase Injections, Bull. Johns Hopkins Hosp. **73**:40-53 (July) 1943.

tion of uricase to "gouty" chickens, made "gouty" by a high protein diet, causes a continued lowering of their plasma uric acid, although they are maintained on the same "gout"-producing diet.

It also "prevents the plasma uric acid level from rising to a 'gouty' level in chickens simultaneously fed a 'gout'-producing diet." [ED. NOTE.—This may be an important finding in the control and prevention of gout.]

Vitamin D.—The controversy still continues as to the use of massive doses of vitamin D for arthritis. Snyder, Squires, Forster and Rudd [506] still claim that results can be secured only by using ergosterol electrically activated prepared by the Whittier process, namely (ertron). They emphasize the fact that ultraviolet-irradiated ergosterol gave bad results in 80 per cent of their cases. It was not tolerated. They gave it to 30 patients for twelve months; 77 per cent were not benefited, 57 per cent refused to continue taking it and 5 only, or 17 per cent, became better. These were different from their results with electrically activated ergosterol. They also report a group of cases [507] in which they used intramuscular injections of electrically activated ergosterol and as much as 1,000,000 to 1,500,000 units proved effective. There were no untoward local or systemic symptoms, and they prevented gastric irritation by using the intramuscular route. They believe that it is perfectly safe, whether given orally or intramuscularly.

[ED. NOTE (L. D. B.).—Ertron is a proprietary preparation which has not been accepted by the Council on Pharmacy and Chemistry of the American Medical Association. The claims of its advantages have been challenged. Before he prescribes the preparation the physician should read some of these challenging reports and should familiarize himself with the toxic manifestations.[507a]]

506. Snyder, R. G.; Squires, W. H., and Forster, J. W.: Six-Year Study of Arthritis Therapy with Special Reference to Pharmacology, Toxicology and Therapeutics, Indust. Med. **12**:291-297 (May) 1943.

507. Snyder, R. G.; Squires, W. H.; Forster, J. W., and Rudd, E.: Therapeutic Value of Electrically Activated Ergosterol When Administered Intramuscularly: Preliminary Report, Indust. Med. **12**:663-668 (Oct.) 1943.

507a. Condol and Ertron Not Acceptable for N. N. R,. report of the Council on Pharmacy and Chemistry, J. A. M. A. **109**:132-133 (July 10) 1937. Freyberg, R. H.: Treatment of Arthritis with Vitamin and Endocrine Preparations: Emphasis of Their Limited Value, ibid. **119**:1165-1171 (Aug. 8) 1942. Freeman, S.: Irradiated Ergosterol Poisoning, correspondence, ibid. **119**:968 (July 18) 1942. Boots, R. H., and Sachs, N. R.: Hope [False] for the Victims of Arthritis, correspondence, ibid. **123**:857 (Nov. 27) 1943.

Klassen and Curtis [508] report the effect of massive doses of vitamin D on calcium and phosphorus metabolism as negligible. "There was no primary disturbance in the calcium and phosphorus metabolism in the patients with atrophic spondylitis or with degenerative arthritis of the spine."

Gold Therapy.—More evidence is constantly appearing as to the beneficial effect of gold therapy on arthritis, as it has been more extensively used. Graham and Fletcher [509] report on 100 patients. Ninety-five received up to 1 Gm. of a gold compound. Of these 67 per cent were improved and 20 per cent obtained moderate improvement. Fifty-four of the 100 had a mild toxic temporary reaction; 4 showed exfoliative dermatitis. They believe the gold valuable, but the good results did not depend on drug therapy alone. "There is evidence that general medical care and protection contribute to favourable progress and lessen likelihood of relapse." They emphasize the fact that there are serious dangers.

Price and Leichtentritt [510] state:

> Aurotherapy should be limited to rheumatoid arthritis, and is most effective in the early stages of the disease. It is also frequently effective in relieving pain and stiffness in advanced cases and is therefore worthy of a trial in these patients. . . . Gold is a toxic drug and should be used only by those having experience with it.

Winkler [511] agrees with them but adds that the results in cases of Marie-Strümpell disease or spondylitis are not especially outstanding, since in most of these cases severe disturbance in the joints and ankylosis are present before treatment is instituted. He believes the gold therapy may be resumed after the toxic symptom subsides. He also notes: "Longer periods of observation are required to determine the permanency of the results."

Cohen and Dubbs [512] review a series of 122 patients who received a total of one hundred and seventy-six courses of intramuscular injections of 1.24 Gm. of aurothiodextrose. Thirty-

508. Klassen, K. P., and Curtis, G. M.: Effect of Massive Doses of Vitamin D on Calcium and Phosphorus Metabolism: Observations on Patients with Atrophic Spondylitis and with Degenerative Arthritis of Spine, Arch. Int. Med. **71**:78-94 (Jan.) 1943.

509. Graham, J. W., and Fletcher, A. A.: Gold Therapy in Rheumatoid Arthritis, Canad. M. A. J. **49**: 483-487 (Dec.) 1943.

510. Price, A. E., and Leichtentritt, B.: Gold Therapy in Rheumatoid Arthritis, Ann. Int. Med. **19**. 70-80 (July) 1943.

511. Winkler, H.: Gold Therapy of Rheumatoid Arthritis, North Carolina M. J. **4**:161-163 (May) 1943.

512. Cohen, A., and Dubbs, A. W.: Treatment of Rheumatoid Arthritis with Gold, New England J. Med. **229**:773-776 (Nov. 18) 1943.

six per cent were much improved, 9 per cent showed no change and 4 per cent were worse. They emphasize the fact that more than one course of treatment is necessary in many cases. They believe that the reduction in toxic reactions was due to the use of fruit juice or vitamin C. They also used extreme caution and gave liver, vitamin B and small doses of the gold compound, 50 mg. They believe that these precautions were the reason for the reduction of untoward reactions.

Freyberg, Block and Levey [513] again report extremely interesting studies on metabolism of gold used in the treatment of rheumatoid arthritis. They found that soluble gold salts were excreted chiefly in the urine while colloidal gold salts were excreted more in the feces.

These complete excretion studies show that gold is retained in large amounts during the period of treatment; the retention ranged from 77 to 88 per cent with the crystalline salts, and often more than 99 per cent with colloidal gold sulphide.

They found that the content of gold in the plasma and the content excreted when the soluble gold sodium thiosulfate was used were the same, whether it was given intravenously or intramuscularly.

Block, Buchanan and Freyberg [514] also report that insoluble gold salts are slowly absorbed. Larger amounts were found in liver and kidney than in other tissues, and the soluble gold salts were excreted by the kidneys and the insoluble by the intestines. [ED. NOTE.—These studies are of inestimable value in increasing knowledge of gold therapy.]

Another valuable contribution is that of Bayles and Hall,[515] in which they demonstrate a way of recording the effect of gold therapy on rheumatoid arthritis. Charts are shown which clearly illustrate the value of tabulating results. This article should be read.

Surgical Treatment.—There is only one article on surgical treatment, by Smith-Petersen, Aufranc and Larson.[516] They suggest that in order to relieve pain surgical operation should be done early before it is too late. Acromioplasty, excision of the head of the radius and excision of the distal end of the ulna are the operative procedures suggested. They point out that early surgical treatment should be done before destruction of the joints is too far advanced to allow maximum benefit from the operation.

Psychologic Aspects.—Emotional disturbances are found in many instances. Swaim [517] draws attention to the fact that they are found in cases of arthritis. The factors of emotional outlets can no longer be avoided. Anger and fear have profound physiologic effects, and investigations in the last ten years show that anxiety and resentment are the two most constant emotional reactions found in arthritic patients. These suggest that maladjusted human relationships are a fundamental problem. He points out that application of spiritual laws will help adjust these conflicts, by "feeding a starved spirit." He believes that physicians should pioneer again in this field of medicine.

Food Allergy.—Food allergy as a possible factor in subacute recurrent arthritis is discussed by Vaughan [518] in a study of a consecutive series of 1,000 adults. Twenty-seven had recurrent subacute involvement of various joints, and for these the causative foods were discovered and attacks prevented by their avoidance. Thirty-two foods were incriminated. He mentions Kahlmeter's 54 cases in which the condition was attributed to allergy, among approximately 5,000 rheumatic patients, Solis-Cohen's 27 cases observed in twenty years in which allergy may have played a part and Hench and Rosenberg's 34 cases of recurrent or palindromic rheumatism. He states:

Although food allergy has not been proved to play a part in the majority of arthritics, there appears to be a small group in whom intermittent hydroarthrosis involving large joints or multiple small joints (with a picture of recurrent subacute rheumatoid arthritis) may be caused by food allergens.

513. Freyberg, R. H.; Block, W. D., and Levey, S.: Metabolism, Toxicity and Manner of Action of Gold Compounds Used in Treatment of Arthritis: Complete Excretion Studies and Comparison of Intravenous and Intramuscular Administration of Some Gold Salts, Ann. Rheumat. Dis. **3**:77-89 (Dec.) 1942.

514. Block, W. D.; Buchanan, O. H., and Freyberg, R. H.: Metabolism, Toxicity and Manner of Action of Gold Compounds Used in Treatment of Arthritis: Studies of Absorption, Distribution and Excretion of Gold Following Intramuscular Injection of Gold Thioglucose and Gold Calcium Thiomalate, J. Pharmacol. & Exper. Therap. **76**:355-357 (Dec.) 1942.

515. Bayles, T. B., and Hall, M. G.: Yardstick for Rheumatoid Arthritis Applied to Patients Receiving Gold Salt Therapy, New England J. Med. **228**:418-421 (April 1) 1943.

516. Smith-Petersen, M. N.; Aufranc, O. E., and Larson, C. B.: Useful Surgical Procedures for Rheumatoid Arthritis Involving Joints of Upper Extremity, Arch. Surg. **46**:764-770 (May) 1943.

517. Swaim, L. T.: President's Address (American Rheumatism Association), Ann. Int. Med. **19**:118-121 (July) 1943.

518. Vaughan, W. T.: Food Allergy as a Possible Factor in Subacute Recurrent Arthritis, Ann. Int. Med. **19**:122-124 (July) 1943.

Myalgia.—Good [519] reports 500 cases of myalgia in the British army. Myalgia is a frequent disease localized in certain anatomic parts of one or more muscles—"myalgic spots."

Myalgia is present in and responsible for the vast majority (according to statistics 95 per cent) of patients suffering from rheumatism; it is not rarely associated with rheumatoid arthritis, osteoarthritis, and commonly with rheumatic fever. . . . It is often of unknown origin—idiopathic myalgia—and mimics visceral and nervous diseases (heart pain, neuralgia or neuritis, sciatica, syndrome of painful feet, etc.)

He describes the myalgic spots—the characteristic feature of myalgia of the neck, shoulder, arm, back, lumbar region, hip and leg. He recommends injection of procaine hydrochloride, which relieves pain in a dramatic way and leads to rapid cure.

519. Good, M.: Five Hundred Cases of Myalgia in British Army, Ann. Rheumat. Dis. **3**:118-138 (Dec.) 1942.

XV. FRACTURE DEFORMITIES

PREPARED BY EUGENE M. REGEN, M.D., NASHVILLE, TENN.; R. BEVERLY RANEY, M.D., DURHAM, N. C.; GLEN BARBER, M.D., CLEVELAND, AND PAUL HARMON, M.D., SAYRE, PA.

The literature for 1943 includes a number of excellent articles on delayed union of fractures and on nonunion, while little emphasis has been placed on malunion. In these articles, all of which are written from a clinical standpoint, attention has been directed about equally to study of the causes of delayed union and nonunion and to exposition of grafting technics, with statistical analyses of the results.

Clinical Studies of Delayed Union and Nonunion.—In a comprehensive article, which merits careful study for full understanding and appreciation, Watson-Jones and Coltart [520] have analyzed a series of 804 fractures of the shaft of the tibia and femur. They state that the test of success in the treatment of a fracture is the quality of the end result rather than the time taken in achieving it. Time is not saved when recovery is accelerated at the cost of permanent disability; a disabled man loses time every day of his life. The period of disability for any fracture is important; of the many factors which influence this period, the most constant is the time taken for the fracture to unite. As a broad generalization, it may be estimated that the duration of total disability is half as long again as the time taken for union of the fracture. The authors disagree with the frequently expressed opinion that fractures of the tibia and femur now unite more slowly than they did several decades ago. They call attention to two great changes which distinguish current treatment of fractures from that of thirty years ago: (1) the demand for roentgenographic evidence of consolidation rather than clinical evidence alone and (2) the current belief that all fractures unite if immobilized long enough and that nonunion is never inevitable. A statement made by Jones in 1912 is recalled by the authors: "We must realize that the academic period of consolidation authoritatively asserted is not accurate, and that bones which appear firm to the hand will yield after many weeks to the incidence of body weight." In addition to the general causes of delayed union, the authors consider three local causes outstandingly important: (1) interrupted immobilization, (2) infection and (3) distraction of the fragments. The authors present tables in which this series of fractures is analyzed from the standpoint of type of injury, location, duration and treatment. In conclusion, the following points are made: Uncomplicated fractures treated by simple manipulation and plaster unite as quickly as in former years; ten to twelve weeks should be the minimal time of immobilization for fractures of the shaft of bones of the lower extremity; interrupted immobilization, distraction, infection and too early weight bearing cause delayed union; excessive traction, with or without distraction, causes marked delay in the healing of fractures of the tibia; operative reduction in skilled hands, even when metal fixation is used, does not delay union; early weight bearing, no matter what type of support is used, should be discouraged, as its benefits are doubtful and its dangers real; fractures of the shaft of the femur should be reduced immediately and light continuous traction used subsequently to maintain length; the time of immobilization for fracture of the femur should not be influenced by the fear of stiffness in the knee joint, as it is due to other causes; infection of fractures and neighboring soft tissues causes serious delay and should be dealt with early but is not a cause of nonunion.

Peterson [521] presents an excellent study of 20 cases of neglected fracture of the femoral shaft

520. Watson-Jones, R., and Coltart, W. D.: Slow Union of Fractures with Study of 804 Fractures of Shafts of Tibia and Femur, Brit. J. Surg. **30**:260-276 (Jan.) 1943.

521. Peterson, L. T.: Neglected Femoral Fractures, J. Bone & Joint Surg. **25**:871-882 (Oct.) 1943.

in which treatment was begun at the Walter Reed General Hospital from several weeks to several months after injury. The article is well illustrated with roentgenograms. For treatment of the uncomplicated fracture suspension traction is the method of choice; its disadvantages are that it requires constant attention, the taking of frequent roentgenograms, nursing care and measures to prevent distraction. Immobilization with plaster alone after primary reduction is condemned because angulation and overriding can occur in the cast. Plaster immobilization should be used for emergency transportation only. Dual pin reduction and fixation are recommended only for relatively simple fractures of the shaft; this method is contraindicated for old fractures, fractures near joints and fractures with large free fragments. The disadvantages of the dual pin method are that it causes discomfort, that the resulting mobility of the knee does not meet expectations and that it may cause osteomyelitis. Open reduction and internal fixation with suitable nonirritating plates and screws are recommended as the treatment of choice where proper facilities are available. This should be done as early as possible, but open reduction does not guarantee union, and proper attention must be paid to blood supply and mechanics, including the avoidance of distraction. When open reduction must be done more than eight weeks after injury, bone grafting is recommended. The preferred method is massive grafting with maximal contact between the graft and the vascular portion of the host. The graft should be fixed with long metal screws. The simultaneous use of a metal plate allows earlier motion of the knee. The author describes several cases of neglected femoral fractures in which later treatment by these methods was successful.

Anderson and Burgess [522] believe that delayed union and nonunion of fractures of the shafts of long bones are usually a result of ill advised treatment, pointing out that in many cases the attending surgeon has failed to observe the basic principles of therapy for fractures. The authors call attention to various ways in which the three commandments for fractures, reduction, immobilization and preservation of blood supply, are daily being broken by conservative skeletal traction and by operative methods. They state that when these principles are efficiently applied over 90 per cent of slow unions are circumvented. They believe that nonunion can be prevented by a simple and practical system which exerts direct skeletal control over both proximal and distal fragments. The authors think that by the use of dual transfixion traction the care of fractures of the extremities is simplified, standardized and made available to all surgeons, regardless of location, who either by preference or by necessity are faced with problems involving fractures. [Ed. Note (E. M. R.).—The authors' criticism is well taken but should be directed more at the attending surgeon and less at the method.]

Anderson and Finlayson [523] point out some of the pitfalls of the transfixion pin method for the treatment of fractures and discuss means of avoiding them. These authors think that complications can in a large measure be prevented and can be limited to a minimum approaching zero when the following technic is carefully employed. Transfixing pins should be inserted through the wide cancellous portion of the bone whenever possible; two pins, two wires or two half-pins at an angle to each other should be placed in each fragment. The transfixions should be used for traction only during the reduction; afterward they should provide "contraction" to keep the ends of the fragments in direct and immobilized contact throughout the whole period of repair. The authors think that employment of these clinically tested principles and insistence on ambulation, with active movement of muscle and joints, will be rewarded by earlier bony union than can be attained by any other method. Complications are said to be usually due not to use but to misuse of transfixion. Common errors arising from fear, unpreparedness or haste include improper placement of the pins, movement between fragments and transfixion, use of transfixion for skeletal traction instead of "contaction" and failure to use transfixion in this way so that the benefits of ambulation may be obtained. [Ed. Note (E. M. R.).—Perhaps greater technical skill is required for the successful application of this method than for the use of more conservative measures.]

Davis [524] reports 6 cases illustrating the frequently observed causal effect of a powerful distracting force in delaying the union of fractures of the long bones. In his cases complete annular tears of the periosteum were demonstrated at operative exposure of the site of fracture. A theoretic explanation of the delayed union is offered, this being "misdirected flow of bone and soft tissue fluid" produced by the annular periosteal rent. In these cases nonunion was treated

522. Anderson, R., and Burgess, E.: Delayed Union and Non-Union: 90 Per Cent Preventable, J. Bone & Joint Surg. **25**:427-445 (April) 1943.

523. Anderson, R., and Finlayson, B. L.: Sequelae of Transfixation of Bone, Surgery **13**:46-54 (Jan.) 1943.

524. Davis, A. G.: Pin Distraction as Cause of Non-Union, J. Bone & Joint Surg. **25**:631-643 (July) 1943.

with onlay grafts which were fixed by long metallic screws. Another type of distraction which may interfere with the healing process in fracture of the shaft of the tibia is emphasized by Stotz.[525] He believes that with tibial fractures, even when the fragments are in perfect apposition, a small gap may result from absorption of bone at the fracture line and that when the fibula is intact such a gap may result in delayed union or nonunion. He is also of the opinion that early union of the fibula, when there is a concomitant fracture of the tibia, may likewise cause delayed union or nonunion of the tibia. In cases in which the intact fibula is responsible for angulation of the tibia, in all cases of oblique tibial fractures in which after six weeks there is still springiness at the site of fracture and in many cases of frank pseudarthrosis, he advocates subperiosteal osteo. omy of the fibula, with removal of from 0.5 to 5 cm. of the bone at a site remote from the tibial fracture. A plaster cast is applied for four to six weeks after operation. The patients begin walking on their casts after the first week. The author has practiced this operation since 1940 and has been satisfied with its results.

An important cause of pseudarthrosis, intraosseous neurofibroma, is emphasized by Green and Rudo.[526] They report a case in which pathologic examination showed neurofibroma to be a factor in the production of the fracture and in the retardation or prevention of union. They recommend that in all cases of "congenital pseudarthrosis" the patient should be examined for stigmas of neurofibromatosis, which include café au lait spots, extraosseous tumors and roentgen evidence of other skeletal defects. In operations on patients with "congenital pseudarthrosis" the possibility that the process may be due to the presence of a neurofibroma should always be considered. If the neurofibroma is the cause of the pseudarthrosis, incomplete excision of the tumor with local recurrence may be a factor in nonunion. [ED. NOTE (R. B. R.).—This differentiation is important and should be kept in mind in all cases of congenital pseudarthrosis.]

Operations for the Treatment of Delayed Union and Nonunion.—Key[527] presents a review of various methods of bone grafting and discusses the indications for each. The operations used to secure union, in order of increasing complexity, are the following: (1) multiple drilling of the fragments, (2) open reduction and internal fixation, with or without multiple drilling of the fragments, (3) step-cut operation and (4) various types of bone grafts, with or without internal fixation. All operations should be followed by adequate external fixation, usually by means of plaster casts. Key found the massive onlay graft to be most useful in the difficult cases; in some instances he used the Phemister modification, in which a massive graft is placed at the site of fracture without internal fixation. The author draws the following conclusions: (1) with the protection of the sulfonamide drugs, operations for delayed union or nonunion may be performed earlier than in the past; (2) the choice of operation depends somewhat on the surgeon in that the procedure should be one which he can execute satisfactorily; (3) the simpler procedures are followed by fewer complications than the more complex measures, but simple procedures will not always solve difficult problems, and (4) a simple operation undertaken early may save time for the patient, avoid a difficult late operation and result in a better limb.

Boyd[528] reports additional experiences with the dual graft technic, in which a cortical bone graft is placed on each side of the shaft at the site of nonunion. The indications and the operative technic are described. Boyd states that osseous union has been secured in 93 to 94 per cent of 511 cases of nonunion in which treatment with the single massive onlay graft, which has been described previously by Henderson, Campbell and Speed, was used. The dual graft, therefore, is reserved for more difficult cases in which there is loss of bone or some other unusual feature such as failure of a previous single graft. Nonunion with loss of substance near a joint is not considered a contraindication. In 18 of the 22 cases described in this report, treatment with the usual dual graft technic was employed. Treatment failed in 1 instance, a case of nonunion with extensive loss of bone near the elbow in which physical therapy was apparently started too early. In 1 case exacerbation of infection occurred but union was nevertheless obtained.

Armstrong[529] believes that the results of fractures of the shaft of the tibia are often imperfect because of a tendency for these injuries to be regarded as trivial, when in reality they

525. Stotz, W.: Resection of Fibula for Pseudarthrosis or Retarded Union of Tibial Fractures, Bull. War Med. **3**:385 (March) 1943.

526. Green, W. T., and Rudo, N.: Pseudarthrosis and Neurofibromatosis, Arch. Surg. **46**:639-651 (May) 1943.

527. Key, J. A.: Choice of Operation for Delayed and Non-Union of Long Bones, Ann. Surg. **118**:665-680 (Oct.) 1943.

528. Boyd, H. B.: Treatment of Difficult and Unusual Non-Unions, with Special Reference to Bridging of Defects, J. Bone & Joint Surg. **25**:535-552 (July) 1943.

529. Armstrong, J. R.: Method of Bone Grafting Tibia and Fibula, Proc. Roy. Soc. Med. **35**:759-760 (Oct.) 1942.

are difficult to reduce and hold satisfactorily. He lists four absolute indications for bone grafting: (1) established nonunion, (2) malunion sufficient to cause serious disability, (3) inadequate reduction by conservative means and (4) extensive loss of bone. He names two relative indications for open operation: (1) delayed union in certain circumstances and (2) grossly unstable fractures. Armstrong advocates the massive sliding graft, or the split bone technic in which a portion of the tibial shaft is resected and reversed.

In another article Armstrong [530] discusses in more detail the massive sliding graft, or the so-called split bone technic, for fractures of the tibia. He exposes the tibia subperiosteally throughout its length, reduces the fracture and holds the fragments temporarily by Lowman clamps. He frequently finds it necessary to refracture or divide the fibula. He then takes the massive graft, of which one third is on the shorter tibial fragment and two thirds on the longer fragment, and reverses it, fixing the longer fragment across the site of fracture with four vitallium screws and placing the shorter fragment in the remaining tibial defect. The alinement is checked by roentgenograms before the wound is closed, and any necessary modifications are made. The fracture is then treated with plaster in the usual way. The author states that this operation is mechanically sound, its technic is simple, it involves only the injured limb and it is followed by rapid and certain union. [ED. NOTE (P. H. H.).—This method has been commonly employed for many years, and since the introduction of vitallium, screws made of that metal have been generally used for fixation of the graft. The conditions and circumstances of the fractures in which the author has employed the method are not mentioned, nor is the extent to which he has employed it. His statement concerning "rapid .and certain union" must be regarded with some reservation.]

Butler,[531] in reporting on a series of 50 patients with fractures of the scaphoid bone for which a peg graft operation was performed, describes the technic. The operations were performed for nonunion, delayed union or recent fracture in which nonunion seemed probable. For 14 patients union was obtained in an average of three months, for 18 union occurred in an average of five months and the remaining 18 were still in plaster or not available for follow-up studies. Owing to the difficulty of placing accurately a large drill in this small bone, the long axis of which lies at an angle of 45 degrees to the transverse plane of the wrist and 40 degrees to the long axis of the limb, as pointed out by Armstrong in 1941, a special arm rest made of aluminum was devised to hold the limb with the long axis of the scaphoid bone vertical. This arm rest is fitted with a shelf to hold a roentgen film in the correct position, so that roentgenograms can be taken at various stages during the operation. Brachial plexus block anesthesia was used. The bone peg was taken from the olecranon. A padded plaster cast was applied to the entire arm immediately after the operation. Twenty-one days later a skin-tight plaster cast was applied to the forearm and molded firmly around the arm and wrist joint almost to the interphalangeal joint of the thumb. The patient was then returned to light duty and came back monthly for supervision. [ED. NOTE (P. H. H.).—A mechanical aid for precision drilling in these difficult operations should be welcome. Its provision and an understanding of its application would seem to be the only drawbacks.]

Vere-Hodge [532] reports the case of a 21 year old flight mechanic in whom pain, weak grip and limited active motion of the wrist following fracture of the scaphoid bone were greatly improved by excision of the proximal fragment.

Thompson [533] describes a "telescoping V osteotomy" for the correction of angular and rotational malalinement in bones which are conoidal in longitudinal section. The smaller fragment is partially telescoped into the larger; the firm apposition of living bone fragments enveloped by periosteum results in considerable stability and prompt union. Plaster casts are used for immobilization. The author reports good results with this technic in diverse situations. While rather severe deformities are shown, the method is no less simple and secure for the treatment of mild ones.

Volkmann's Ischemic Paralysis.—Albert and Mitchell [534] discuss the various theories of the pathogenesis of Volkmann's paralysis and describe 3 cases of vascular injury in the leg, ischemia of the muscles of the anterior tibial compartment, drop foot and massive late calci-

530. Armstrong, J. R.: Bone-Grafting in Treatment of Fractured Tibia and Fibula, Lancet **2**:188-191 (Aug. 14) 1943.

531. Butler, A. A.: Bone Pegging Carpal Scaphoid, Proc. Roy. Soc. Med. **35**:760-761 (Oct.) 1942.

532. Vere-Hodge, N.: Early Excision of Avascular Fragment of Fractured Carpal Navicular Bone, Proc. Roy. Soc. Med. **35**:764 (Oct.) 1942.

533. Thompson, V. P.: Telescoping V Osteotomy: General Method for Correcting Angular and Rotational Disalinements, Arch. Surg. **46**:772-779 (May) 1943.

534. Albert, M., and Mitchell, W. R. D.: Volkmann's Ischemia of the Leg, Lancet **1**:519-522 (April 24) 1943.

fication and formation of an abscess. The ischemia was thought to be of the Volkmann type. The authors suggest that ischemia is due either to temporary arterial obstruction or to venous occlusion and that the resulting deformity depends chiefly on muscle tone in the affected part. The possible effect of skin-tight plaster casts and the importance of surgical intervention to relieve tension in the anterior compartment of the leg are stressed. Splinting will relieve the deformity and prevent a part of it but will not restore power to the muscles. The chalky deposits and the abscesses of the late stage may require surgical removal. In the established case, a shoe for drop foot with a spring brace and lateral uprights will improve function. It is suggested that more of these cases will be observed under wartime conditions and that calcification may be demonstrated in old cases of ischemic palsy of the forearm.